Evaluation Report ERC2010-05

Flumioxazin

(publié aussi en français)

16 June 2010

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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Canada

HC Pub: 100124

ISBN: 978-1-100-14154-1 (978-1-100-14155-8)
Catalogue number: H113-26/2010-5E (H113-26/2010-5E-PDF)

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Overview

Registration Decision for Flumioxazin

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for the sale and use of Flumioxazin Technical, Flumioxazin 51WDG Herbicide to control weeds in numerous crops and Flumioxazin 0.25G Herbicide to control weeds in container grown ornamentals.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

Although the risks and value have been found acceptable when all risk reduction measures are followed, the applicant must submit additional scientific information as a condition of registration.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Flumioxazin Technical, Flumioxazin 51WDG Herbicide and Flumioxazin 0.25G Herbicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.hc-sc.gc.ca.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's *(a)* efficacy; *(b)* effect on host organisms in connection with which it is intended to be used; and *(c)* health, safety and environmental benefits and social and economic impact."

What Is Flumioxazin?

Flumioxazin is the active ingredient in the end-use products Flumioxazin 51WDG Herbicide and Flumioxazin 0.25G Herbicide. Flumioxazin 51WDG Herbicide is used to control weeds in numerous crops and Flumioxazin 0.25G Herbicide is used to control weeds in container grown ornamentals.

Flumioxazin inhibits a specific enzyme in sensitive plants. Sensitive plants emerging from soil treated with flumioxazin become necrotic and die shortly after exposure to sunlight.

Health Considerations

Can Approved Uses of Flumioxazin Affect Human Health?

Flumioxazin is unlikely to affect your health when used according to proposed label directions.

Potential exposure to flumioxazin may occur through diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur, and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g., children and nursing mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when using flumioxazin products according to label directions.

Flumioxazin technical grade active ingredient and the end-use products, Flumioxazin 0.25G Herbicide and Flumioxazin 51WDG Herbicide showed a potential for slight toxicity by the inhalation route in animals. Because of this, the label statement CAUTION - POISON is required. Flumioxazin did not cause cancer in animals and was not genotoxic. There was also no indication that flumioxazin caused damage to the nervous system. There were significant effects on fetal development. The first signs of toxicity in animals given daily doses of flumioxazin over longer periods of time were effects on the blood, and liver and bile systems. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

When flumioxazin was given to pregnant animals, effects on the developing fetus were observed at doses that were not toxic to the mother, indicating that the fetus was more sensitive to flumioxazin than the adult animal. Because of this observation, extra protective measures were applied during the risk assessment to further reduce the allowable level of human exposure to flumioxazin.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that women 13-49 years old, the most sensitive population group to flumioxazin, are expected to be exposed to ≤5.5% of the acceptable daily intake, and children 1-2 years old, the population group that would ingest the most flumioxazin relative to body weight, are expected to be exposed to ≤3.7% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from flumioxazin is not of concern for all segments of the population. Flumioxazin is not carcinogenic; therefore, a chronic cancer dietary risk assessment is not required.

A single dose of flumioxazin is not likely to cause acute health effects in the general population (including infants and children). An aggregate (food and water) dietary intake estimate for females 13-49 years old used less than 15% of the acute reference dose, which is not a health concern.

The *Food and Drugs Act (FDA)* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for FDA purposes through the evaluation of scientific data under the *Pest Control Products Act (PCPA)*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout the United States using flumioxazin on potatoes, dry bulb onions, soybeans, apples, pears, peaches, plums, cherries, blueberries, grapes, strawberries, and asparagus were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this Evaluation Document.

Occupational Risks From Handling Flumioxazin 51WDG Herbicide or Flumioxazin 0.25G Herbicide

Occupational risks are not of concern when Flumioxazin 51WDG Herbicide or Flumioxazin 0.25G Herbicide are used according to the label directions, which include protective measures.

Farmers, custom applicators, or ornamental nursery operators who mix, load or apply Flumioxazin 51WDG Herbicide or Flumioxazin 0.25G Herbicide as well as field workers re-entering freshly treated fields, bare ground non-crop areas, and nurseries can come in direct contact with flumioxazin residues on the skin. Therefore, the labels specify that anyone mixing/loading and applying Flumioxazin 51WDG Herbicide or Flumioxazin 0.25G Herbicide must wear the personal protective equipment (PPE) recommended. The label also requires that workers do not enter treated crop areas until 12 hours after application. Also, no entry is allowed into treated, non-crop bare-ground use areas until the sprays have dried. Taking into consideration these label statements, the number of applications, and the expectation of the exposure period for handlers and workers, it was determined that exposures to these individuals are not a concern.

For bystanders, exposure is expected to be much less than that of workers. Therefore, health risks to bystanders are considered not to be of concern.

For people who enter treated fields for "pick-your-own" activities, exposure is expected to be short-term even though this activity may be performed once or several times per year. Taking into consideration the label requirements, the risk to people that enter treated fields to pick apples, pears, highbush blueberries, or strawberries is not of concern.

Environmental Considerations

What Happens When Flumioxazin Is Introduced Into the Environment?

Flumioxazin enters the environment when used on various crops and ornamentals for weed control. Flumioxazin is non-persistent to moderately persistent with the main route of transformation in the terrestrial environment being biotransformation in soil. Flumioxazin is not expected to volatilise nor leach significantly. No major transformation products of flumioxazin were identified in the aerobic soil laboratory studies.

Although the use pattern for fluioxazin does not include direct application to water, the possibility that aquatic systems will be exposed to flumioxazin and its major transformation products, directly or indirectly, cannot be ruled out. Flumioxazin can enter the aquatic environment through spray drift and runoff from treated fields. In aquatic systems, flumioxazin transforms rapidly via hydrolysis and anaerobic biotransformation to a number of major transformation products. Phototransformation can also contribute to the dissipation of flumioxazin from the water layer in the photic zone. Hydrolysis is the main route of transformation in water and the rate increases with increasing pH.

Major transformation products of flumioxazin were identified in the aquatic anaerobic fate studies. These transformation products may be persistent and may accumulate in aquatic systems. The fate of these transformation products has not been fully characterised since an aerobic aquatic biotransformation study was not submitted. Further discussion regarding these transformation products occurs in the Science Evaluation section of this document.

The risk to the environment was assessed for both flumioxazin end-use products, Flumioxazin 0.25G Herbicide and Flumioxazin 51WDG Herbicide.

At the proposed application rate and use pattern, Flumioxazin 0.25G Herbicide, a granular-based formulation, is not expected to pose a risk to terrestrial organisms. A risk to small mammals was identified through the incidental ingestion of granules, however, the end-use product formulation does not contain any formulants that are likely to attract mammals, nurseries may already have measures in place to control for rodents and the application instructions require that that treatment area is irrigated immediately after treatment, thereby dissolving the granules. Therefore, exposure to Flumioxazin 0.25G Herbicide granules is likely to be minimised. At the proposed application rate, Flumioxazin 0.25G Herbicide is not expected to pose a risk to aquatic invertebrates, fish and amphibians on an acute or chronic basis. Flumioxazin 0.25G may pose a risk to algae and vascular plants on an acute basis if runoff containing flumioxazin runs into water bodies. To reduce this potential risk, advisory runoff statements are included on the label.

In the terrestrial environment, Flumioxazin 51WDG Herbicide, at the proposed application rate and use pattern, may pose a risk to vascular plants and insect parasitoids. These risks may be mitigated by applying spray buffer zones and label statements. A reproductive risk to small mammals was identified at the screening level assessment. Further refinement and characterization of the risk by examining the application method, timing of application, availability of vegetation both on and off the field and the foraging behaviour of small mammals indicated that the reproductive risk to small mammals is unlikely to manifest itself in the field. No risk was identified to earthworms, bees, birds and wild mammals on an acute basis.

In the aquatic environment, Flumioxazin 51WDG Herbicide, at the proposed application rate and use pattern, is not expected to pose a risk to freshwater and marine aquatic invertebrates, fish and amphibians on an acute or chronic basis. A risk to freshwater algae and vascular plants was identified from exposure to runoff and drift. The risks identified from drift may be mitigated by applying spray buffer zones and label statements. To reduce the potential risk from runoff, advisory statements are included on the label. Additional data will be requested to further characterize this risk and address uncertainties.

Value Considerations

What Is the Value of Flumioxazin 51WDG Herbicide?

Flumioxazin 51WDG Herbicide provides pre-emergence control or suppression of specific broadleaf and grass weeds in non-crop areas, field-grown coniferous ornamental trees, field-grown deciduous ornamental trees, soybean, dry-bulb onion, pome fruit (apple and pear), grape, highbush blueberry, stone fruit (peach, cherry, nectarine, plum, and apricot), asparagus, potato and strawberry.

With the exception of ornamentals, Flumioxazin 51WDG Herbicide represents a new mode of action for pre-emergence weed control for all uses listed on the label.

What Is the Value of Flumioxazin 0.25G Herbicide?

Flumioxazin 0.25G Herbicide provides pre-emergence control or suppression of specific broadleaf weeds in container-grown ornamentals.

Weed management is critical in container-grown ornamental production. Containers that are over-run with weeds become less marketable, as consumers want clean, weed-free product. There are very few herbicides registered for use in container-grown ornamentals.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Flumioxazin 51WDG Herbicide and Flumioxazin 0.25G Herbicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Since there is a concern with users coming into direct contact with flumioxazin on the skin or through inhalation of spray mists, anyone mixing, loading, applying, and involved in clean-up or repair activities with Flumioxazin 51WDG Herbicide or Flumioxazin 0.25G Herbicide must wear the recommended personal protective equipment (PPE). Standard label statements to protect against spray drift during application are included on the label. A restricted entry interval (REI) was required for post-application handline irrigation after over-the-top application to field-grown coniferous trees and trees grown for reforestation.

Environment

Mitigative measures are required to protect sensitive terrestrial and aquatic habitats from the use of flumioxazin. These mitigative measures include precautionary statements on the label regarding environmental hazards and the directions for use as well as appropriate buffer zones to protect sensitive habitats from spray drift.

What Additional Scientific Information Is Being Requested?

Although the risks and value have been found acceptable when all risk-reduction measures are followed, the applicant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation of this Evaluation Report or in the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information to the PMRA by September 30, 2012.

Environment

- The $\log K_{OW}$ is required for the major transformation products identified in the aquatic environment;

- An analytical method for the analysis of the major transformation products in aquatic systems is required:

- Either one of the following two studies is required:
  - an aerobic aquatic biotransformation study, or
  - an aerobic water/sediment biotransformation study;

- ecotoxicology studies on daphnids, rainbow trout and aquatic vascular plants conducted with transformation products expected to accumulate in the aquatic environment are conditionally required, pending the results of the aerobic aquatic biotransformation study;

- An overspray study is required to characterise the risk from drift and overspray to aquatic plants.

Chemistry

- Analytical data from at least five batches of technical grade active ingredient representing full-scale production.

- Mass spectra or chromatograms confirming identity of active ingredient and impurities.

- Storage stability data for the end-use products representing at least one year of storage at ambient conditions.

Value

For Flumioxazin 51WDG Herbicide:

- Five efficacy trials conducted on coarse-textured soils with less than 5% OM (organic matter) for each of the following seven weed species: redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, and dandelion.

- Five efficacy trials conducted on medium-textured soils with less than 5% OM for each of the following eight weed species: common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, and dandelion.

- Three to four efficacy trials conducted in potato for each of the following four weed species: common lamb's-quarters, redroot pigweed, eastern black nightshade, and hairy nightshade.

- Three to four efficacy trials conducted on muck soil for each of the following six weed species: common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, and hairy nightshade.

- Three soybean crop tolerance trials conducted on medium-textured soils with 3-5% OM.

- Three asparagus crop tolerance trials conducted on coarse-textured soils with < 5% OM and an additional three trials conducted on medium-textured soils with < 5% OM.

- Three crop tolerance trials conducted on apricot for both broadcast application to dormant trees and directed applications to vegetative trees.

- Three to four crop tolerance trials conducted on strawberry for both broadcast application to dormant plants, and hooded or shielded applications to row middles prior to fruit set.

- Two to three soybean rotational crop trials conducted on medium-textured soils with 3-5% OM.

Other Information

As these conditional registrations relate to a decision on which the public must be consulted,[3] the PMRA will publish a consultation document when there is a proposed decision on applications to convert the conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

The test data cited in this Evaluation Report (i.e. the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

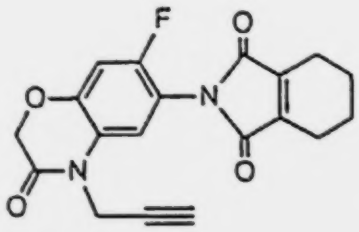
[3] As per subsection 28(1) of the *Pest Control Products Act*.

Science Evaluation

Flumioxazin

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Flumioxazin
Function	Herbicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	7-fluoro-6-[(3,4,5,6-tetrahydro)phthalimido]-4-(2-propynyl)-1,4-benzoxazin-3(2*H*)-one
2. Chemical Abstracts Service (CAS)	2-[7-fluoro-3,4-dihydro-3-oxo-4-(2-propynyl)-2*H*-1,4-benzoxazin-6-yl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione
CAS number	103361-09-7
Molecular formula	$C_{19}H_{15}FN_2O_4$
Molecular weight	354.33 g/mole
Structural formula	
Purity of the active ingredient	97.9% (96.0- 100%)

1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

Technical Product—Flumioxazin Technical

Property	Result
Colour and physical state	Yellowish-brown powder
Odour	Odourless
Melting range	201.83 to 203.83°C
Boiling point or range	Not applicable
Density	1.5136 g/mL at 20°C

Property	Result
Vapour pressure	2.41×10^{-6} mm Hg at 22°C
Henry's law constant at 20°C	6.252×10^{-7} atm·m^3/mol
Ultraviolet (UV)-visible spectrum	pH — λ max (nm) 1.9 — 218 and 290 6.8 — 216 and 290 10.0 — 216 and 290
Solubility in water	1.79 mg/L at 25°C
Solubility in organic solvents at 20°C (g/100 mL)	Solvent — Solubility Ethyl acetate — 1.78 Methanol — 0.156 Hexane — 2.47×10^{-3} N-octanol — 1.63×10^{-2} Acetone — 1.70 Acetonitrile — 3.23 Dichloromethane — 19.1 Tetrahydrofuran — 5.38
n-Octanol-water partition coefficient (K_{ow})	pH — log Kow 5.93 — 2.55
Dissociation constant (pK_a)	The active ingredient does not dissociate.
Stability (temperature, metal)	The test substance was determined to be stable at 54°C for 14 days in contact with steel and when exposed to sunlight for 100 hrs.

End-Use Product—Flumioxazin 0.25G Herbicide

Property	Result
Colour	Gray
Odour	Odourless
Physical state	Solid
Formulation type	Granular
Guarantee	0.25% (0.22-0.28%)
Container material and description	High density Polyethylene (HDPE) bottle or paper bag with an aluminium foil barrier
Density	0.778 g/mL
pH of 1% dispersion in water	8.3
Oxidizing or reducing action	The product does not have any oxidizing or reducing actions.
Storage stability	Not yet provided. The study is in progress.

Property	Result
Corrosion characteristics	Not yet provided. The corrosion characteristic study is in progress.
Explodability	The product is not explosive.

End-Use Product—Flumioxazin 51WDG Herbicide

Property	Result
Colour	Beige
Odour	Odourless
Physical state	Solid
Formulation type	Water Dispersible Granules
Guarantee	51.1% (49.6-52.6%)
Container material and description	HDPE bottle
Density	0.532 g/mL
pH of 1% dispersion in water	5.9
Oxidizing or reducing action	The product does not have any oxidizing or reducing actions.
Storage stability	Not provided. The study is in progress.
Corrosion characteristics	Not provided. The corrosion characteristic study is in progress.
Explodability	The product is not explosive.

1.3 Directions for Use

1.3.1 Flumioxazin 51WDG Herbicide

Flumioxazin 51WDG Herbicide provides pre-emergence control or suppression of common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, and dandelion in soybean, dry-bulb onion, asparagus, highbush blueberry, grape, pome fruit (apple and pear), stone fruit (peach, cherry, nectarine, plum, and apricot), potato, strawberry, field-grown coniferous ornamental trees, and field-grown deciduous ornamental trees. The product is applied once or twice per growing season at a rate of 54, 71 or 140 g a.i./ha (Table 1.3.1.1) in coarse-textured soils with < 5% organic matter (OM), or at a rate of 54, 107 or 214 g a.i./ha in medium-textured soils with < 5% OM, or at a rate of 71 g a.i./ha in muck soils. The number of applications and application rate varies by crop. This product cannot be used in any other soil types. Flumioxazin 51WDG may be applied as a broadcast treatment or as a directed hooded spray with ground application equipment only. This product may not be used for aerial application.

Table 1.3.1.1 Weed Control Claims for Flumioxazin 51WDG Herbicide

Soil Conditions	Herbicide Rate	Weeds Controlled
Coarse-textured soils < 5% OM	71 or 140 g a.i./ha	**Control:** common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, dandelion
Medium-textured soils < 5% OM	107 or 214 g a.i./ha	
Coarse- and medium-textured soils < 5% OM	54 g a.i./ha	**Suppression:** common lamb's-quarters, redroot pigweed, eastern black nightshade, hairy nightshade
Muck soils	71 g a.i./ha	**Suppression:** common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade
Do not apply on mineral soils with > 5% OM, or on fine-textured soils.		

1.3.2 Flumioxazin 0.25G Herbicide

Flumioxazin 0.25G Herbicide provides pre-emergence control of hairy bittercress and liverwort and suppression of common groundsel and common chickweed in container-grown ornamentals. The product is to be applied once or twice per growing season at a rate of 210 or 420 g a.i./ha (Table 1.3.2.1) as a broadcast treatment with drop or rotary type granular application equipment.

Table 1.3.2.1 Weed Control Claims for Flumioxazin 0.25G Herbicide

Herbicide Rate	Weeds Controlled
210 g a.i./ha	**control:** hairy bittercress/snapweed
420 g a.i./ha	weeds listed above plus **control:** liverwort **suppression:** common groundsel, common chickweed

1.4 Mode of Action

Flumioxazin 51WDG Herbicide and Flumioxazin 0.25G Herbicide

Flumioxazin belongs to the N-phenylphthalimide chemical family. The mode of action (Group 14) is the inhibition of the enzyme protoporphyrinogen oxidase (PPO). This enzyme is part of the chlorophyll biosynthesis pathway, and its inhibition leads to a loss of chlorophyll and carotenoids, and irreversible damage to cell membrane function and structure. Sensitive plants emerging from soils treated with the herbicide flumioxazin become necrotic and die shortly after exposure to sunlight.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in flumioxazin technical have been provided and assessed to be precise and accurate.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulations has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

A gas chromatography method with nitrogen-phosphorus detection (GC-NPD) was developed and proposed for data gathering and enforcement purposes in plant commodities. This method fulfilled the requirements with regards to specificity, accuracy and precision at the specified method limit of quantitation. Acceptable recoveries (70-120%) were obtained in plant matrices. Radioavalidation of the method was provided for grape and peanut samples from the metabolism studies. The proposed enforcement method was successfully validated by an independent laboratory. Methods for residue analysis are summarized in Appendix I, Table 1.

High-performance liquid chromatography methods with tandem mass spectrometry (HPLC-MS/MS) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant and animal matrices and environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

The PMRA conducted a detailed review of the toxicological database for flumioxazin. The database is complete, consisting of the full array of laboratory animal (in vivo) and cell culture (in vitro) toxicity studies currently required for health hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to characterize the toxicity of this pest control product.

Technical flumioxazin is of low acute toxicity by the oral, dermal and inhalation routes in Sprague Dawley rats. It was non-irritating to minimally irritating when applied to the skin and eyes of New Zealand White rabbits. Results of skin sensitization testing in Hartley guinea pigs using the maximization method were negative.

The flumioxazin end-use products Flumioxazin 0.25G Herbicide and Flumioxazin 51WDG Herbicide are of low acute toxicity by the oral and dermal routes in Sprague Dawley rats. By the inhalation route in Sprague Dawley rats, they were found to be slightly toxic. They were minimally irritating when applied to the skin and eyes of New Zealand White rabbits. Results of skin sensitization testing in Hartley guinea pigs using the Maximization method were negative.

Absorption and excretion of single or repeated oral doses of flumioxazin was very rapid. Approximately 80-90% of the administered dose was absorbed at 1 mg/kg bw, and excretion was almost complete, with feces as the principal route of clearance. Within 48 hours, more than 96% of the administered dose (both high and low doses) was detected in the urine and feces. At 100 mg/kg bw, feces was still the principal route of clearance, but the peak plasma concentration was only 20 times that of the low dose suggesting a large reduction in absorption. Tissue residues declined rapidly, with the highest levels occurring in the blood, liver, kidneys and heart at the low dose or thyroid, liver, kidney, lung, spleen and heart at the high dose.

Several metabolites were isolated, identified and characterized from urine, feces and bile of rats treated with radiolabelled flumioxazin. Flumioxazin was almost completely metabolized by hydroxylation, conjugation, and cleavage. No quantitative sex differences were observed. Approximately ten metabolites were identified among the 35 total peaks in the thin layer chromatography results. Unchanged parent was a very minor component of recovered radioactivity except for the fecal extracts of the high dose group where the parent comprised 50% of the total recovered radioactivity.

A short-term dermal study showed no skin irritation in any of the test groups after repeated applications of flumioxazin to the shaved skin of albino rats. The only observed effect was very slight hematotoxicity, similar to that seen in the oral dosing studies, but to a lesser extent. The small changes in hematocrit and hemoglobin were not considered toxicologically adverse.

In subchronic and chronic toxicity studies, flumioxazin produced specific target organ toxicity in the blood (rats) and liver (dogs). Flumioxazin induces hematotoxicity in rats by blocking the heme biosynthesis pathway. The heme deficiency leads to a regenerative anemia. There is some evidence of hematotoxicity in mice, but rats are far more susceptible. Rats also exhibited increased heart and spleen weights, and chronic nephropathy. Toxicity in the dog was limited to liver effects such as increased liver weight, proliferation and dilatation of smooth endoplasmic reticulum in hepatocytes, proliferation of bile ducts, increased cholesterol, phospholipids, and alkaline phosphatase, plus hyperplasia of the connective tissue adjacent to the gall bladder. Chronic dosing of mice at levels approaching the limit dose produced minor effects in the liver that did not exhibit a dose response pattern and are believed to be coincidental. There was no common toxicity observed between mice, rats, or dogs. There was no evidence of oncogenicity in either rats or mice. Duration of dosing did not significantly increase the degree of toxicity observed, however, similar effects were seen at lower doses in the chronic study.

No evidence of mutagenic potential of flumioxazin was observed in vitro with the Ames bacterial mutation test. There was no evidence of mutagenic potential of flumioxazin in an unscheduled DNA synthesis assay with rat hepatocytes. Under the conditions of an in vitro clastogenicity study in the presence of metabolic activator at test substance precipitating dose levels, using Chinese hamster lung fibroblasts, a positive result was obtained for chromatid breaks and exchanges. When tested for chromosome aberrations in vivo, rats showed no genetic damage. On the whole, based on the data presented, flumioxazin was not considered to be genotoxic.

There was evidence of increased susceptibility of the young in oral and dermal rat teratology studies. Parental rats showed no toxicological effects, while pups exhibited ventricular septal defects (VSD) in the heart and an increase in the total number of cardiovascular anomalies. There was also a decreased number of live fetuses, an increase in fetal death and resorptions, decreased fetal weights, wavy ribs, and curvatures of the scapula and ulna. Similar effects were observed in both the oral and dermal studies, though the lowest observed adverse effect level (LOAEL) was higher in the dermal study. The deaths and malformations in rats at maternally non-toxic doses presented a significant concern, which is accounted for in the risk assessment. The fetal death and cardiovascular malformations occurred frequently in several of the available developmental and mechanistic studies, with a well defined dose response relationship. Rabbit dams exhibited decreased body weight gain and food consumption at the highest dose tested, while the fetuses showed no adverse effects at any dose level.

In a two-generation reproductive toxicity study, the no observed adverse effect level (NOAEL) and LOAEL were again higher in parental animals than in pups. In the absence of maternal toxicity, there was a decrease in live pups per litter, a decrease in pup viability at day 4, and a decrease in pup body weight. At the next higher dose, adults exhibited decreased body weight, body weight gain, and food consumption, increased mortality, a red substance in the vaginas, yellow livers with bile stasis, centrilobular necrosis in the liver, and decreased absolute, but not relative male reproductive organ weights and brain weights. At this dose level, the number of resorptions increased and mating indices decreased.

A number of mechanistic studies for developmental toxicity were performed with small groups of rats, rabbits, and/or mice. The goal of these studies was to determine the mechanism and the timing of embryonic toxicity. Additionally, several in vivo and in vitro hematotoxicity studies were performed to examine interspecies differences in blood toxicity. The mechanistic studies provided were sufficient to establish a probable toxicological mode of action for flumioxazin, particularly with respect to developmental toxicity. Inhibition of the enzyme protoporphyrinogen oxidase (PPO) impacts heme synthesis which leads to anemia. In the fetus, the resulting hypoxia causes growth retardations and death, heart enlargements, and decreased protein synthesis. The enlarged hearts likely lead to VSD, while the protein deficiencies may contribute to the ulnar and scapular malformations and the wavy ribs. The degree of PPO inhibition of flumioxazin was assessed in the livers of several species in vitro. In general, the approximate grading of sensitivity to PPO inhibition, from greatest to least, was rat, mouse, human, rabbit, dog. Additionally, two other structurally related herbicides were tested in pregnant rats and rabbits for their VSD potential and their relative levels of PPO inhibition. There was a direct relationship between PPO inhibition and higher incidences of VSD. In addition, fetal concentrations of flumioxazin and its metabolites were examined in a toxicokinetics study. The results showed that only a small amount of the administered dose crosses the placenta, yet this exposure was sufficient to produce malformations and mortality thus strengthening the concern with regards to the potential for both qualitative and quantitative sensitivity in offspring.

Results of the acute and chronic tests conducted on laboratory animals with flumioxazin and its associated end-use products Flumioxazin 0.25G Herbicide and Flumioxazin 51WDG Herbicide, as well as the toxicological endpoints selected for the human health risk assessment, are summarized in Tables 2, 3 and 4 in Appendix I.

PCPA Hazard Considerations

For assessing risks from potential residues in food or from products used in or around residential areas or schools, the Pest Control Products Act (PCPA) requires the application of an additional 10-fold factor to threshold effects. This factor should take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children and potential pre- and post-natal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database, extensive data were available on flumioxazin including two developmental toxicity studies in rats (oral and dermal), a developmental toxicity study in rabbits, a two-generation reproduction study in rats, and several supplemental developmental mechanistic studies in rats, rabbits, and mice.

In terms of pre- and post-natal toxicity, there is evidence of increased qualitative and quantitative sensitivity of rat fetuses and pups compared to the adult animals via both oral and dermal routes. In both rat developmental toxicity studies, the fetuses exhibited death as well as visceral and skeletal malformations at doses that were shown to be non-toxic to the dams. The two-generation rat reproduction study also showed a decrease in the number of live pups and decreased pup viability in the absence of maternal toxicity. Toxicokinetic studies in pregnant rats showed that flumioxazin crosses the placenta and enters the fetus within two hours of dosing and a very small amount of flumioxazin in the fetus (relative to the total dose given to the dam) is sufficient to

cause the observed effects. Both malformations and mortality occurred following a single dose of flumioxazin. As developmental malformations represent a serious endpoint, a reduction in the PCPA factor is not warranted for relevant populations (i.e. females 13-49).

3.2 Determination of Acceptable Daily Intake

General Population

The recommended acceptable daily intake (ADI) for the general population for flumioxazin is 0.02 mg/kg bw/day, based on the calculation shown below. The chronic rat toxicity study was considered to be the most appropriate study to assess chronic dietary exposure. The NOAEL was 1.8 mg/kg bw/d, based on hematotoxicity at 18.0 mg/kg bw/d. The standard uncertainty factors of 10-fold each have been applied to account for intraspecies variability in toxicological responses and interspecies extrapolation. Since the in utero effects are not a relevant endpoint for the general population, the PCPA factor as discussed in the PCPA Hazard Considerations section can be reduced to 1-fold. Therefore, the composite assessment factor (CAF) is 100.

The ADI proposed for the general population is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{1.8 \text{ mg/kg bw/day}}{100} = 0.02 \text{ mg/kg bw/day}$$

Females 13-49

A separate ADI for females of reproductive age is warranted to protect for gestational effects and is set at 0.003 mg/kg bw/d as seen in the calculation below. In this case, the oral developmental toxicity study in rats was considered to be the most relevant. The NOAEL was 3 mg/kg bw/d based on cardiovascular anomalies, particularly VSD, at 10 mg/kg bw/d as well as increased fetal mortality and skeletal malformations at 30 mg/kg bw/d. The standard uncertainty factors of 10-fold each have been applied to account for intraspecies variability in toxicological responses and interspecies extrapolation. As outlined in the PCPA Hazard Considerations section above, the PCPA factor of 10 is retained to provide additional protection for unborn children due to quantitative and qualitative sensitivity of the young and seriousness of the endpoint. Therefore, the CAF is 1000.

The ADI proposed for females 13-49 is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{3.0 \text{ mg/kg bw/day}}{1000} = 0.003 \text{ mg/kg bw/day of flumioxazin}$$

The two-generation rat reproduction study had an offspring and a reproductive NOAEL of 6.3 mg/kg bw/d based on decreased live pups per litter in the F_2 generation, decreased pup viability at day four in both generations, and decreased pup body weight in the F_1 generation. The ADI is protective of these observed effects.

3.3 Determination of Acute Reference Dose

General Population
An acute reference dose for the general population was not established as there were no acute endpoints of concern for this group.

Females 13-49
The most appropriate study for selecting a toxicity endpoint for acute dietary exposure was the developmental toxicity study in rats, with a NOAEL of 3.0 mg/kg bw/day, based on an increase in cardiovascular anomalies, particularly VSD at 10 mg/kg bw/day. The recommended acute reference dose (ARD) for females of reproductive age for flumioxazin is 0.003 mg/kg bw, based on the calculation shown below. The standard uncertainty factors of 10-fold each have been applied to account for intraspecies variability in toxicological responses and interspecies extrapolation. As the developmental effects observed can occur following a single exposure, the PCPA factor of 10 is retained to provide additional protection for unborn children due to quantitative and qualitative sensitivity of the young and seriousness of the endpoint. Therefore, the CAF is 1000.

$$\text{ARD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{3.0 \text{ mg/kg bw/day}}{1000} = 0.003 \text{ mg/kg bw of flumioxazin}$$

3.4 Occupational Endpoints

Dermal
For short and intermediate term dermal exposures, the fetal cardiovascular malformations in the dermal rat developmental study at 100 mg/kg bw/day provide the most appropriate endpoint. The NOAEL for this endpoint was 30 mg/kg bw/day. The standard uncertainty factors of 10-fold each have been applied to account for intraspecies variability in toxicological responses and interspecies extrapolation. As the worker population could include pregnant and lactating women, it is necessary to ensure adequate protection of the fetus or the nursing infant who may be exposed via their mother. In light of concerns regarding pre- and post-natal toxicity (as outlined in section 3.2), a 10-fold uncertainty factor was applied to these endpoints. Therefore, the target MOE is 1000.

Inhalation
For short and intermediate term inhalation exposures, the fetal cardiovascular malformations in the oral rat developmental study at 10 mg/kg bw/d provide the most appropriate endpoint. The NOAEL for this endpoint was 3 mg/kg bw/d. The standard uncertainty factors of 10-fold each have been applied to account for intraspecies variability in toxicological responses and interspecies extrapolation. As the worker population could include pregnant and lactating women, it is necessary to ensure adequate protection of the fetus or the nursing infant who may be exposed via their mother. In light of concerns regarding pre- and post-natal toxicity (as outlined in section 3.2), a 10-fold uncertainty factor was applied to these endpoints. Therefore, the target MOE is 1000.

Occupational and Residential Risk Assessment
Occupational exposure to flumioxazin is characterized as short- to intermediate-term duration for mixer, loader, applicator and post-application worker, and is predominantly by the dermal and inhalation routes. There were no exposure data available for intense contact with treated bare ground of soil. However, worker exposure to treated soil was calculated using default transferable turf residue values.

3.4.1 Toxicological Endpoints

3.4.1.1 Dermal Absorption

An acceptable *in vivo* rat dermal absorption study, following EPA guidelines was reviewed. However, all dermal exposure estimates were compared to a dermal endpoint determined from a rat developmental study. Therefore, a dermal absorption value for the purposes of the present assessments was not required.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to flumioxazin during mixing, loading and application. Dermal and inhalation exposure estimates for workers were generated from the Pesticide Handlers Exposure Database (PHED) version 1.1. The PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates. To estimate exposure for each use scenario, appropriate subsets of A and B grade data were created from the database files of PHED for dry flowable open mix/loading coupled with application equipment of groundboom, low- and high-pressure handwand, backpack, and right-of-way sprayers. The PHED estimate for the granular formulation mixer/loader exposure was the open mix/load, granule scenario, coupled with the application equipment of push-type and hand-cranked rotary spreaders, broadcast granular spreader, and dispersal by hand. The maximum application rate is 214 grams active ingredient per hectare, depending on soil characteristics for Flumioxazin 51WDG Herbicide, and maximum application rate of 420 grams active ingredient per hectare for Flumioxazin 0.25G Herbicide.

Chemical-specific exposure data for assessing human exposures during pesticide handling activities were not submitted.

Exposure to workers mixing, loading and applying Flumioxazin 51WDG Herbicide is expected to be short-term duration (up to 30 days per season), or intermittent intermediate-term duration (up to 6 months) including potential post-emergence burndown uses, and to occur primarily by the dermal and inhalation routes. Exposure estimates were derived for mixer/loaders/applicators applying Flumioxazin 51WDG Herbicide for pre-emergence control of annual broadleaf and grassy weeds in field-grown ornamentals, deciduous trees, and coniferous trees including Christmas trees and trees produced for reforestation, soybean (post-emergence burndown also), dry bulb onion, pome fruit (apple and pear), grape, highbush blueberry (post-emergence burndown also), stone fruit (peach, prune, sweet and sour cherry) (post-emergence burndown

also), asparagus (post-emergence burndown also), and to maintain bare ground non-crop areas (including railroad beds, under guard rails, above-ground pipelines, parking and storage areas, plant sites, substations, pumping stations, oil yards/substations and tank farms, airports, brick yards, industrial plant sites, lumber yards and storage areas, around farm buildings, along fence rows, road surfaces and gravel shoulders, in and around ornamental nurseries and farms, and military installations) using ground application equipment.

Short-term exposure duration is expected for Flumioxazin 0.25G Herbicide use on container-grown ornamentals, by ground spreader equipment or by manual dispersal.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption factor of 1, (the occupational NOAEL being based on an endpoint determined from a dermal study). Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 70 kg adult body weight (Table 3.4.2.1.1.).

Exposure estimates were compared to a route-specific toxicological end point (no observed adverse effects level) to obtain the margin of exposure (MOE). The target MOE is 1000.

The initial exposure estimates were derived with mixers/loaders/applicators wearing a long-sleeved shirt, long pants, chemical-resistant gloves, goggles or a faceshield, socks and shoes. Mixer/loader/applicator exposure refinement was necessary when the target margin of exposure was not met for a specific equipment scenario. Where appropriate, further mitigation measures were based on a prescribed maximum amount of product handled per day. Additional PPE, engineering controls, or restricted amount of product handled per day, were considered in achieving the target MOE (Tables 3.4.2.1.1 and 3.4.2.1.2).

Table 3.4.2.1.1. Mixer, loader, and applicator summary exposure and risk assessment.

Crop Scenario	Application Equipment (Notes 1,2, and 3)	Maximum Application Rate (g a.i./ha)	ATPD[A] (ha/day) Or Amount of a.i. handled per day (kg a.i./d)	Dermal Unit Exposure[B] (µg ai/kg ai)	Inhalation Unit Exposure[B] (µg ai/kg ai)	Combined MOE[C,D]
Flumioxazin 51 water dispersible granule formulation						
Crop, and non-crop bare ground areas	Backpack	214	0.765 (kg a.i./d)	2689	63.12	1642
	Right-of-Way sprayer		3.542 (kg a.i./d)	532	6.02	1000
	Groundboom, closed cab		23.4 (kg a.i./d)	89	1.08	1000
	Groundboom, open cab		22.5 (kg a.i./d)	96	1.12	1000
	Low-pressure handwand		0.161 (kg a.i./d)	11568	142	1007
	High-pressure handwand		0.518 (kg a.i./d)	2545	152	1001
Flumioxazin 0.25 Granular formulation						
Container-grown ornamentals	Open-cab, Solid Broadcast (granular) spreader (M/L+A)	420	5 (ha/day)	28.93	3.8	14900
	Push-type rotary spreader (M/L/A)		2 (ha/day)	2034	3.68	1207
	Hand-crank (Belly grinder) spreader (M/L/A)		0.68 (ha/day)	5548.67	126.9	1079
	dispersed by hand (A)		0.08 (ha/day) (0.00336 kg a.i./d)	55422.5	605	1017

Note 1: Assumption that mixer, loader, and applicator are the same person

Note 2: Backpack scenario was based on extrapolation of Liquid, open pour, backpack scenario summed with dry flowable, open pour, mix/load, which was not expected to underestimate spraying of water dispersible granules, providing there is continuous agitation of mixture.

Note 3: High-pressure handwand scenario was based on extrapolation of Liquid, open pour, high-pressure scenario summed with dry flowable, open pour, mix/load, which was not expected to underestimate spraying of water dispersible granules, providing there is continuous agitation of mixture.

A. Area-treated-per-day default database, 2004

B. Scenario dermal and inhalation unit exposures were used from the Pesticide Handlers Exposure Database, version 1.1
Push-type spreader PHED scenario unit exposure of 6448.49 µg ai/kg ai, with **no head or neck data**, single layer and **no gloves**, A,B, and C grade data, which was corrected for head surface area of 1205 cm^2 (for head and neck) as a proportion of whole body area of 18440 cm^2: 6448.49+ ((6448.49x(1205/18440)) = 6870 µg ai/kg ai. Coveralls over single layer **and gloves** exposure was calculated as a 75% protection factor of the total PHED value of 6448.49 µg ai/kg ai, which includes hands. This was not expected to overestimate protection, as chemical-resistant gloves, if able to be included, are rated as a 90% protection factor (Recommended Protection Factors, January 2000) and the calculated head exposure added: (6448.49 x 0.25)+ ((6449.49 x (1205/18440)) = 2034 µg ai/kg ai.

C. (Dermal or Inhalation) Exposure Estimates

$$= \frac{\text{[Application Rate X Area treated per day] or [Amount of a.i. handled per day] x PHED Exposure (µg ai/kg ai handled) x Absorption Factor}}{\text{bw (70kg)}}$$

where,
body weight = 70 kg
Dermal absorption assumed to be 100%, since NOAEL based on a dermal study, therefore factor = 1;
Inhalation absorption assumed to be 100% systemically available, therefore factor =1;

Occupational endpoints: Short and Intermediate duration exposure: Dermal, based on the rat dermal developmental study NOAEL of 30 mg/kg bw/day; inhalation, based on the rat oral developmental study NOAEL of 3 mg/kg bw/day; a target MOE of 1000 for both routes.

$$\text{MOE} = \frac{\text{(Dermal or Inhalation) NOAEL (mg/kg bw/d)}}{\text{(Dermal or Inhalation) exposure estimates (mg/kg/day)}}$$

D. Combined MOE calculated according to SPN2003-04

Table 3.4.2.1.2. Personal Protective Equipment Instructions for Flumioxazin 51WDG Herbicide.

Follow mixer/loader and applicator scenario, as appropriate in the chart below. In addition, wear coveralls over long-sleeved shirt and long pants, chemical-resistant gloves, socks and shoes, goggles or faceshield, during clean-up and repair activities.

<table>
<tr><th rowspan="2">Equipment</th><th colspan="2">Personal Protective Equipment</th><th rowspan="2">Maximum amount of product handled per day (kg)</th></tr>
<tr><th>Mixer/Loader</th><th>Applicator</th></tr>
<tr><td rowspan="2">Groundboom</td><td rowspan="2">Chemical-resistant coveralls and chemical-resistant gloves, socks and shoes, and goggles or faceshield</td><td>Open cab: Coveralls over long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves, and respirator with a NIOSH/MSHA/BHSE approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH/MSHA/BHSE approved canister approved for pesticides</td><td rowspan="2">44 kg</td></tr>
<tr><td>Closed cab: Long-sleeved shirt, long pants, socks and shoes. (No gloves are required, but must be available for maintenance activities)</td></tr>
<tr><td>Right-of-Way sprayer</td><td colspan="2">Chemical-resistant coveralls and chemical-resistant gloves, socks and shoes. Mixers and loaders must also wear goggles or faceshield.</td><td>7.0 kg</td></tr>
<tr><td>Backpack or High-pressure handwand equipment</td><td colspan="2" rowspan="2">Coveralls over long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, and respirator with a NIOSH/MSHA/BHSE approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH/MSHA/BHSE approved canister approved for pesticides. Mixers and loaders must also wear goggles or faceshield.</td><td>1.2 kg</td></tr>
<tr><td>Low-pressure Hand-held Equipment</td><td>0.315 kg</td></tr>
<tr><td>Airblast</td><td colspan="3">Not for use with airblast equipment</td></tr>
</table>

Do not enter or allow entry into treated areas until the sprays have dried in non-crop bare ground use areas.

Do not enter or allow worker entry into treated areas during the restricted entry interval of 12 hours for all crop uses.

For field-grown coniferous trees, including Christmas trees and trees produced for reforestation: Do not enter treated areas for handline irrigation for a period of 6 days after over-the-top application.

Personal protective equipment and use restrictions for Flumioxazin 0.25G Herbicide are:

Personal Protective Equipment
Loaders, applicators, and other handlers must wear coveralls over long-sleeved shirt and long pants, chemical-resistant gloves made of any waterproof material such as polyethylene or polyvinyl chloride, shoes and socks.

Restrictions
The maximum amount of product handled per day for hand dispersal must not exceed 13 kg product/day.

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers re-entering crops or areas treated with flumioxazin from scouting, transplanting, grafting/propagating, trellising, staking, mowing, cultivation, spraying other pesticides, pruning, thinning, irrigating, harvesting, moving plants or container-grown plants. Given the nature of activities performed, dermal contact with treated surfaces is expected. Post-application inhalation exposure is not expected as the water dispersible granule formulation has low vapour pressure and is unlikely to volatilize, and the active will be soil-bound once irrigation has occurred or sufficient moisture is present. The duration of exposure is considered to be short- to intermediate-term, and the primary route of exposure for workers re-entering treated areas would be through the dermal route.

Dermal exposure to workers entering foliar treated areas is estimated by coupling dislodgeable foliar residue values with activity-specific transfer co-efficients. Activity transfer coefficients are based on Agricultural Re-entry Task Force data, of which Valent USA Corporation is a member. Chemical-specific dislodgeable foliar residue data were not submitted. As such, a default dislodgeable foliar residue value of 20% of the application rate on the day of application and 10% daily dissipation was used in the exposure assessment. Dermal surface area available for contact with treated bare ground was considered not to be underestimated by the post-application foliar transfer co-efficients for the activities conducted. Dermal surface area of contact in military installations was calculated based on coveralls over long-sleeved shirt and long pants.

Exposure estimates were compared to the relevant toxicological endpoint to obtain the margin of exposure (MOE). The target MOE was 1000. All post-application tasks assessed for field, nursery (field or container-grown) crops or bare ground non-crop areas were considered acceptable (Tables 3.4.2.2.1 and 3.4.2.2.2).

Table 3.4.2.2.1. Exposure and risk estimate for post-application re-entry to treated field and nursery crops, and non-crop bare ground areas by workers.

Application site scenario	Tasks	Maximum application rate (g ai/ha)	Number of applications	Transfer Co-efficient (cm^2/hr)[A]	DFR value ($\mu g/cm^2$)	Dermal Adherence factor ($\mu g/cm^2$)	Days after last application	Exposure Duration [B] (hours)	Daily Dose [C,D] (mg/kg bw/day)	MOE [E]	Restricted entry interval [F] (days)
over-the-top application to hardened off Coniferous trees (based on foliar application)[F]	Soil-contact tasks: Transplanting or harvesting trees for market, hand weeding, (mowing not conducted on treated ground)	214	2 (56 day interval)	1500			0	8	0.0734	**409**	9 days transplanting tasks not likely to be performed so soon after application;
	Handline irrigation			1100	0.4292	Not applicable			0.0540	**556**	6 days
	Scouting, training (staking, tying)			500					0.0245	1227	none
	hand weeding			100					0.0049	6116	none
Bare ground, crop and non-crop areas, and in and around ornamental nurseries	Occupational dermal contact with treated crop (30 day spray interval) and non-crop ground (60 day spray interval) are not quantified; expected to be mitigated by the use of clothing appropriate to crop-specific tasks (pre-emergence to crop and burndown (see scouting, above), be no more than military use, and therefore considered not to be of concern										none
Bare ground, non-crop area; ground-directed, on Military Installations	All activities	214	2 (60 day interval)	6200	Not applicable	1.0	0	12	1.9×10^{-3}	1.58×10^{4}	none

A. Transfer co-efficients were used from the Interim Revisions to Policy 003.1, and Transfer Coefficients for Orchard Tree Crops and Christmas Trees (2004)

B. Typical work day duration of 8 hours. Recommended revisions to the Standard Operating Procedures (SOPs) for Residential Exposure Assessments, revised February 22, 2001.

C. Daily Dose estimates from foliar application were calculated using the following formula. Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments, December 1997:

$$\frac{\text{DFR Value } (\mu g/cm^2) \times \text{Transfer Coefficient } (cm^2/hr) \times \text{Hours Worked per Day (hr)} \times \text{Conversion Factor } (1mg/1000\mu g) \times DA}{\text{Body Weight}} \qquad \text{Equation 1}$$

Where, DFR value for a single application = application rate g ai/ha x 10^6 µg/g x 10^{-8} ha/cm^2 x soil or foliar dislodgeable fraction on the day of application.
Dissipation is considered not to occur on the same day as application.
Based on a dermal absorption (DA) value of 100%, based on a NOAEL for a rat dermal study. Default of 20 % dislodgeable foliar residue on day of application and 10% daily dissipation rate following foliar application to Conifers. Body weight is considered to be 70kg for an adult;

D. Using an amended (accounting for multiple applications) equation from the Risk Assessment Guidance for Superfund, Volume I, Human Health Evaluation Manual (Part A) ("RAGS", EPA, 1989) presents an equation used to estimate exposure from dermal contact with soil (as stated in Technical Guidance Manual, Mid Atlantic Risk Assessment, Office of Superfund Programs, Hazardous Waste Management Division, United States Environmental Protection Agency), the Part E, Supplemental Guidance for Dermal Risk Assessment) Interim, and Exposure Factors Handbook, 1997 edition:

$$AD = \left(\left(\sum_{n=1,2}^{N} (CS \times (1\text{-}DD)^{(DALA)_n}\right)\right) \times CF \times SA \times AF \times ABS \times EF \times ED)/(BW \times AT) \qquad \text{Equation 2}$$

Where, AD = Absorbed dose (mg/kg bw/day)
$\sum$ = summation of residue from n number of applications
N = Total number of applications ; there are 2 in total
n = number of application
CS = Chemical concentration in soil (mg/kg)) = 2.14 µg ai /cm^2 x 1/cm (depth) = 2.14 µg ai/cm^3 x 0.67 cm^3/g soil = 1.434 µg ai/g soil (=mg ai/kg soil)
DD = Daily dissipation rate = assumed to be 2.42% = 0.0242, based on the laboratory soil dissipation study half-life of 28.66 days (value provided from EAD)
DALA = Days after last application = spray interval = minimum of 30 days for fruit crops (56 days for field-grown ornamentals; 60 days for non-crop areas, including military installations); entry of 0 days after last application
CF = Conversion factor (10^{-6} kg/mg)
SA = Skin surface area available for contact (cm^2/event) = 6200 cm^2/h
AF = Soil-to-skin adherence factor (mg/cm^2) = 1 for military; 0.2 for workers
ABS = Absorption factor (unitless) = 100% = 1
EF = Exposure frequency (events/day) = 8 hours/day for crop work; 12 hours/day for military
ED = Exposure duration (one day)
BW = Body weight (kg)
AT = Averaging time (period over which exposure is averaged-days) = 1 day

E. MOE = NOAEL/ Daily dose, for dermal exposure, based on a dermal NOAEL of 30 mg/kg bw/day from the rat developmental study; with a target MOE of 1000
F. None = no REI time in addition to the product REI of 12 hours; otherwise the product REI is included with the task-specific REI.

Table 3.4.2.2.2. Exposure and risk estimate for post-application re-entry after treating ornamental containers with Flumioxazin 0.25G Herbicide.

Sub-population	Tasks	Maximum application rate [A] (g ai/ha)	Number of applications	Body Surface Area available for soil contact[B] (cm^2/hr)	Absorbed Dose[C] (mg/kg bw/day)	MOE [D]	Restricted entry interval (days)
Adult worker (including females 13-49, dermal)	Transplanting, digging plants, other high-contact soil-related tasks; moving and transporting contain-grown ornamentals	420	2	1500	1.11×10^{-4}	2.70×10^{5}	none

A) Maximum application rate = 420 g ai/ha = 4.2 µg/cm^2.

B). Body surface area of 1500cm^2/h was used for minimum surface area of hands + lower forearms (904 cm^2 + (1173cm^2/2)) from International Harmonisation Position Paper of Methodology Issues, 1999, Appendix II, and tree harvesting from Transfer Coefficients for Orchard Tree Crops and Christmas Trees (2004).

C). Using the equation from the Risk Assessment Guidance for Superfund, Volume I, Human Health Evaluation Manual (Part A) ("RAGS", EPA, 1989) presents an equation used to estimate exposure from dermal contact with soil (as stated in Technical Guidance Manual, Mid Atlantic Risk Assessment, Office of Superfund Programs, Hazardous Waste Management Division, United States Environmental Protection Agency), the Part E, Supplemental Guidance for Dermal Risk Assessment) Interim, and Exposure Factors Handbook, 1997 edition.

Assumption 1: All active ingredient (ai) is sequestered in top 1 cm of soil at time of post-application entry;
Soil density = 0.67 cm^3/g soil (U.S. EPA Standard Operating Procedures for Residential Exposure Assessments)
Soil concentration = 4.2 µg ai /cm^2 x 1/cm (depth) = 4.2 µg ai/cm^1 x 0.67 cm^3/g soil = 2.814 µg ai/g soil (= mg ai/kg soil)

Assumption 2: Post-application entry occurs the same day as the second application, therefore no degradation, dissipation, but adsorption to soil achieves saturation;

Assumption 3: That the treated soil is dry when entry occurs;

Assumption 4: That 100% of active residue contained in the soil-to-skin adherence (i.e. flux), is considered a monolayer, is available for skin contact and is rapid compared to dermal absorption (instantaneous), and not the rate-limiting step;

Assumption 5: An event is 1 hour, and each 1 hour interval represents a fresh soil loading.

$$AD = \sum_{n=1,2}^{N} ((CS \times (1\text{-}DD)^{(DALA)_n}) \times CF \times SA \times AF \times ABS \times EF \times ED)/(BW \times AT) \qquad \text{Equation 2}$$

Where,
AD = Absorbed dose (mg/kg bw/day)
CS = Chemical concentration in soil (mg/kg) = 2.814 mg ai/kg soil
N = Total number of Applications are 2
n = for 1 to N number of applications,
DD = Daily total dissipation and degradation rate = assumed to be 2.42% = 0.0242, based on the laboratory soil dissipation study half-life of 28.66 days (data provided by EAD)
DALA = Days after last application = re-entry 77 days after first application; re-entry 0 days after second application
CF = Conversion factor (10^{-6} kg/mg)
SA = Skin surface area available for contact (cm^2/event) = Transfer co-efficient (cm^2/h) = 1500
(based on Interim Golf Course and Sod Farm Transfer Coefficients, 2003)
AF = Soil-to-skin adherence factor (mg/cm^2) = 0.2
ABS = Absorption factor (unitless) = 100% = 1
EF = Exposure frequency (events/day) = 8 hour workday
ED = Exposure duration = 1 day
BW = Body weight (kg) = 70kg
AT = Averaging time (period over which exposure is averaged-days) = 1

D. MOE = NOAEL/ Daily dose, for dermal exposure, based on a dermal NOAEL of 30 mg/kg bw/day from the rat developmental study; with a target MOE of 1000.

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

There are no domestic class products; therefore, a residential handler assessment was not required.

3.4.3.2 Post-application Exposure and Risk

There are no domestic class products, or commercial products for application in residential areas. Therefore, a residential post-application assessment was not required.

3.4.3.3 Bystander Exposure and Risk

Bystander exposure should not be of concern since the potential for drift is expected to be minimal. Application to agricultural and ornamental crops, and bare ground, non-crop areas, is limited to when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature, application equipment and sprayer settings.

Table 3.4.3.3.1. Post-application exposure and risk assessment for dermal contact with treated ground for treated non-crop bare-ground areas, and pickers at pick-your-own (U-pick) operations after use of Flumioxazin 51WDG.

Sub-population by crop	Tasks	Maximum application rate (g ai/ha)	Number of applications	Transfer Co-efficient (cm^2/hr)[A]	Body Weight (kg)	Daily Dose [C, D,E,F] (mg/kg bw/day)	MOE [G]	Restricted entry interval (days)
Adult non-worker (contact with treated ground)	Dermal contact with treated	214	2	904	70	4.06×10^{-6}	7.4×10^{6}	none
Children (average of 3 years of age, dermal) from treated ground	bare ground (hands only)			385	15	8.7×10^{-6}	3.7×10^{6}	none
Child (1-3 years of age)(Incidental oral ingestion of soil)	Oral ingestion not quantified, as no acute reference dose required for this sub-population							

Note: Highbush Blueberry, application ground-directed at crop base; PHI = 7 days

A. TC value of 500 (whole body exposure of adult) was adjusted for average body surface area of Child (1-6 years-old) 7860 cm^2, compared to adults, 18440 cm^2. International Harmonisation Position Paper on Methodology Issues, PMRA, US EPA, CalDPR, 1999

B. A single application per year for highbush blueberry

C. Expected exposure duration for bystanders entering pick-your-own operation of 2 hours. Recommended revisions to the Standard Operating Procedures (SOPs) for Residential Exposure Assessments. Revised 2001.

D. A dermal absorption value of 100% incorporated, due to a dermal NOAEL of 30 mg/kg bw/day from the rat developmental study, at application rate of 107 g a.i./ha, for soil-directed application around highbush blueberry, and exposure duration of 2 hours. Modified use of Risk Assessment Guidance for Superfund, Volume I, Human Health Evaluation Manual (Part A) ("RAGS", EPA, 1989) presents an equation used to estimate exposure from dermal contact with soil (as stated in Technical Guidance Manual, Mid Atlantic Risk Assessment, Office of Superfund Programs, Hazardous Waste Management Division, United States Environmental Protection Agency), the Part E, Supplemental Guidance for Dermal Risk Assessment) Interim, and Exposure Factors Handbook, 1997 edition, to account for the pre-harvest interval of 7 days.

N

$$AD = \sum_{n=1,2} ((CS \times (1-DD)^{(DALA)_n})) \times CF \times SA \times AF \times ABS \times EF \times ED)/(BW \times AT) \quad \text{Equation 2}$$

Where, AD = Absorbed dose (mg/kg bw/day)
CS = Chemical concentration in soil (mg/kg) = 2.14 µg ai /cm^2 x 1/cm (depth) = 2.14 µg ai/cm^3 x 0.67 cm^3/g soil = 1.434 µg ai/g soil (=mg ai/kg soil)
DD = Daily dissipation rate = 2.42% = 0.0242, from the laboratory soil dissipation study half-life (DT_{50}) of 28.66 days (value provided from EAD)
DALA = Days after last application = 56 days spray interval; and re-entry interval of 7 days after second application.
CF = Conversion factor (10^{-6} kg/mg)
SA = Skin surface area available for contact (cm^2/event) = Transfer co-efficient (cm^2/h) = 500 (from U.S. EPA Policy 003.1)
AF = Soil-to-skin adherence factor (mg/cm^2) = 0.2
ABS = Absorption factor (unitless) = 100% = 1
EF = Exposure frequency (events/day) = 2 hours/day for picking
ED = Exposure duration (one day)
BW = Body weight (kg); adult 70kg; Child 15kg
AT = Averaging time (period over which exposure is averaged-days)

E. MOE = NOAEL/ Daily dose, for dermal exposure, based on a dermal NOAEL of 30 mg/kg bw/day from the rat developmental study; with a target MOE of 1000

3.4.4 Aggregate Exposure and Risk for Pick-Your-Own Operations

Pick-your-own scenarios were considered for highbush blueberry, strawberry, pear, peach, cherry, and apple crops. Exposure associated with post-application harvesting and picking includes dermal exposure from contact with treated ground, and oral exposure by dietary intake. There was no acute hazard identified for children, or the general population. An aggregate assessment was not required for these sub-populations. The sub-population at risk was the female 13-49 age-group. Contact related to harvesting or fruit picking activity with crops having pesticide residues was not quantifiable; however, application is ground-directed, and shielded if necessary, to minimize spraying of foliage and edible fruit. Dermal contact with treated ground (represented by soil) was estimated for bare-ground contact for non-workers. Exposure was considered minimal, not to be of concern, and aggregate assessments were not conducted.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for risk assessment and enforcement in plant products is flumioxazin. In animal commodities, the residue definition for enforcement is flumioxazin and the metabolites 3-OH-flumioxazin and 4-OH-flumioxazin in ruminant commodities; and flumioxazin in poultry commodities. The residue definitions for risk assessment in animal commodities are the following: in ruminant muscle and fat, flumioxazin and the metabolites 4-OH-flumioxazin and Metabolite C; in ruminant meat byproducts, flumioxazin and the metabolites 482-HA, SAT-482, 3-OH-flumioxazin, 4-OH-flumioxazin and Metabolites B, C and F; in milk, flumioxazin and the metabolites 482-HA and Metabolites B and C; in poultry commodities, flumioxazin and the metabolites APF, 3-OH-flumioxazin, 4-OH-flumioxazin, 4-OH-flumioxazin-SA, THPA, 4-OH-THPA and OH-flumioxazin (see Figure 1, Table 5 for chemical structures). The GC/NPD enforcement analytical methodology was valid for the quantification of flumioxazin residues in plant commodities. The residues of flumioxazin are stable when stored in a freezer at -20°C for 198 days in representative crops, including grapes, soybeans, cherries, and potatoes. The residues of flumioxazin are stable when stored in a freezer at -20 °C for 68 days in representative processed crop fractions, including prunes, grape juice, raisins, apple wet pomace and apple

juice. Raw agricultural commodities (RACs) were processed. Given that no quantifiable residues were detected in the RACs and processed commodities, it was not possible to calculate processing factors for these fractions. Supervised residue trials conducted throughout the United States using end-use products containing flumioxazin at the proposed rate and exaggerated rates in or on potato, dry bulb onion, soybean, apple, pear, peach, plum, cherry, blueberry, grape, strawberry and asparagus are sufficient to support the proposed MRLs.

3.5.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.0), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following assumptions were made in a basic chronic analysis: 100% crop treated, default processing factors, and residues of flumioxazin in all crops at MRL values. The basic chronic dietary exposure from all supported flumioxazin food uses (alone) for the total population, including infants and children, and all representative population subgroups is 3.7% of the acceptable daily intake (ADI). The basic chronic dietary exposure from all supported flumioxazin food uses (alone) for females 13-49 years old is 5.0% of the ADI. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to flumioxazin from food and water is 1.1% (0.000227 mg/kg bw/day) of the ADI for the total population, and 5.5% (0.00164 mg/kg bw/day) of the ADI for females 13-49 years old. The highest exposure estimate is for children 1-2 years at 3.7% (0.000742 mg/kg bw/day) of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. The following assumptions were made in a refined acute analysis: 100% crop treated, default processing factors, residues in all crops at MRL values, and a zero value for all animal commodities. The basic acute dietary exposure (food alone) from all supported flumioxazin food uses is estimated to be 12.7% (0.000381 mg/kg bw/day) of the ARfD for females 13-49 years old (95th percentile, deterministic). Aggregate exposure from food and water is considered acceptable: 14.2% of the ARfD for females 13–49 years old.

3.5.3 Aggregate Exposure and Risk

The aggregate risk for flumioxazin consists of exposure from food and drinking water sources only; there are no residential uses. Aggregate risks were calculated based on acute (females 13-50 years old) and chronic endpoints. There was no acute endpoint identified for the general population, including infants and children.

3.5.4 Maximum Residue Limits

Table 3.5.1 Proposed Maximum Residue Limits

MRLs (ppm)	Foods
0.02	Tuberous and Corm Vegetables (Crop Subgroup 1C); Bulb Onion Subgroup (Crop Subgroup 3-07A); Soybean, seed; Pome fruits (Crop Group 11), Stone fruits (Crop Group 12); Bushberries, except lowbush blueberries (Crop Subgroup 13-07B); Small fruit vine climbing, except fuzzy kiwifruit (Crop Subgroup 13-07F); asparagus
0.07	Low growing berries (Crop Subgroup 13-07G)

For information on MRLs in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in animal and plant matrices, analytical methodologies, field trial data, and the acute and chronic dietary risk estimates are summarized in Appendix I, Tables 1, 5 and 6.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Flumioxazin enters the environment when used as a preemergent herbicide on various crops and ornamentals. Flumioxazin is non-persistent to moderately persistent with the main route of dissipation in the terrestrial environment being biotransformation in soil. A large portion of the applied radioactivity was determined to be non-extractable in the soil biotransformation studies (up to 74% under aerobic conditions and up to 60% under anaerobic conditions). This non-extractable radioactivity was determined to be primarily flumioxazin transformation products containing the phenyl moiety. Phototransformation will not contribute significantly to the dissipation of flumioxazin in the terrestrial environment. No major transformation products of flumioxazin were identified in the aerobic soil laboratory studies. The Henry's law constant indicates that flumioxazin is expected to be slightly volatile from moist soil and water surfaces, however, flumioxazin was not found to be volatile in the laboratory studies. The column leaching study showed low to very high mobility in soils and flumioxazin meets some of the Cohen criteria for leaching. However, since flumioxazin has a low water solubility, does not dissociate, is rapidly hydrolysed in water and did not show significant vertical movement in the field dissipation and field lysimeter studies, leaching in soil under typical use and soil conditions will be minimal.

The groundwater ubiquity score (GUS) (Gustafson, 1989) was not used to estimate the leaching potential of this chemical since a batch equilibrium study, a study to derive Kd and K_{OC} values was not conducted with flumioxazin. The Kd and K_{OC} values reported were estimated from the column leaching study and were used to describe the mobility, but the validity of using these values to derive a calculated GUS score is questionable.

Groundwater modeling, which utilized a scenario that would result in the largest amount of leaching indicated that low levels of flumioxazin may be detected in groundwater. However, no significant vertical movement of flumioxazin in the field dissipation and field lysimeter studies was observed. As a result, flumioxazin is not considered to be of significant concern regarding leaching.

Flumioxazin may enter the aquatic environment through spray drift or runoff, however, it is not expected to persist in aquatic environments. Flumioxazin rapidly transforms via hydrolysis, phototransformation and anaerobic biotransformation to a number of major transformation products.

Hydrolysis rates are pH-dependent, with the rate increasing with increasing pH. The hydrolysis studies submitted showed increasing concentrations of several major transformation products at study termination. The major transformation products, APF, THPA and 482-HA are expected to be more mobile than the parent.

In water exposed to light, flumioxazin phototransforms rapidly to 482-PHO, 482-PHO-ISO, 482-PHO-DC, THPA, adipic acid and unknown 1. All major transformation products, except for THPA, adipic acid and unknown 1, were intermediates, as they decreased in concentration prior to study termination. THPA, adipic acid and unknown 1 continued to increase in concentration until study termination, which indicates they may be persistent in the aquatic environment.

In water under anaerobic conditions, flumioxazin transformed rapidly to APF, THPA, DAPF, SAT-482-HA, HPA, UP-1 and bound residues containing the phenyl moiety. SAT-482-HA, DAPF and HPA, unique to the anaerobic biotransformation studies, were stable and/or continuing to increase in concentration at study termination. The fate of these transformation products has not been fully characterised since an aerobic aquatic biotransformation study was not submitted. The information provided indicates that they may persist in the aquatic environment. Additional information, such as the $\log K_{OW}$ and either an aerobic water biotransformation study or an aerobic water/sediment biotransformation study is requested to further characterize the fate of the transformation products in the environment.

The structure and the percent detected of the major and minor transformation products of flumioxazin are presented in Table 7 in Appendix I. Data on the fate and behaviour of flumioxazin and its transformation products are summarized in Tables 8 and 9 in Appendix I.

Exposure concentrations for various environmental media, such as food, water and soil were estimated based on the use patterns of both flumioxazin end-use products, Flumioxazin 51 WDG Herbicide and Flumioxazin 0.25G Herbicide.

4.2 Effects on Non-Target Species

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on Terrestrial Organisms

Risk of flumioxazin and its related end-use products to terrestrial organisms was based upon the use pattern for each end-use product and the evaluation of toxicity data for the following (Appendix 1, Table 10):

- One earthworm species, one bee species and six other arthropods representing invertebrates;
- Two bird and two mammal species representing vertebrates (acute, short-term dietary, reproduction, developmental gavage);
- Ten crop species representing non-target vascular plants; and

- An acute oral toxicity study for honeybees, toxicity studies for beneficial arthropods and an acute oral toxicity study for mallard ducks were not submitted. These studies were submitted to and reviewed by the EU. The results were summarized in the EU monograph and considered in this assessment.

The screening level RQs for Flumioxazin 51WDG Herbicide were assessed based on the maximum application rate (two applications of 214 g a.i./ha) for earthworms, honeybees, predators and parasites, birds, small mammals and terrestrial plants as these organisms may be exposed through direct application, contact with treated material or from ingestion of contaminated food. The assessment is addressed in this Section, 4.2.1, and in Section 4.2.2.

The screening level risk assessment for Flumioxazin 0.25G Herbicide (two applications of 420 g a.i./ha) was assessed for earthworms exposed through the ingestion of treated soil and for birds and small mammals through the ingestion of granules. Since Flumioxazin 0.25G Herbicide is a granular pesticide, exposure to honeybees and predatory and parasitic arthropods through direct application and ingestion of contaminated food are not expected and were therefore not included in the risk assessment. This is addressed in Section 4.2.3.

Flumioxazin 51WDG Herbicide

Terrestrial Invertebrates

An earthworm toxicity study for flumioxazin was submitted. No significant mortality or decrease in bodyweight was observed at the highest concentration tested. The NOEC was 61 mg a.i./kg soil based on body weight and mortality. Risk quotients calculated for the screening level did not exceed the level of concern (Appendix I, Table 12). The use of flumioxazin is not expected to pose a risk to earthworms.

The following results were summarized in the EU monograph and were considered in this assessment. The acute contact and acute oral LD_{50} values for flumioxazin were > 105 µg ai/bee and > 100 µg ai/bee, respectively. Both of these represent the highest dose tested with no sub-acute effects noted at any concentration tested. According to Atkins et al. (1981),the LD_{50} in micrograms per bee (µg/bee) can be converted to the equivalent application rate in kg/ha by multiplying µg/bee by 1.12. After conversion, the acute oral LD_{50} values is > 112 kg a.i./ha and the acute contact LD_{50} value is > 117.6 kg a.i./ha. An RQ was calculated using the following equation: LD_{50}/EEC; where the EEC is the proposed maximum seasonal application rate of 2 x 0.214 kg a.i./ha. The RQs calculated and presented in Appendix I, Table 12 do not exceed the level of concern. The use of flumioxazin is not expected to pose an acute risk on a contact or oral basis. The studies reviewed by the EU indicated that for most predator and parasite species, flumioxazin did not elicit an effect when applied at 0.6 g ai/ha (1.4 times higher than the proposed application rate). A 75% increase in effects, increase mortality and/or decreased parasitism, was reported for the parasitic wasp indicating that the use of flumioxazin may exceed the level of concern for insect parasitoids.

Terrestrial Vertebrates

Acute and reproductive toxicity studies using mallard duck and bobwhite quail were submitted. The acute bird toxicity studies (cral and dietary) showed no treatment-related mortalities occurring at the highest dose tested in both study types. The reproduction studies demonstrated that no avian reproductive effects were noted for the bobwhite quail at the highest dose tested. In the reproductive study with the mallard duck, a slight effect on egg production was noted at the highest dose tested and the NOEC was therefore established at 250 mg a.i/kg diet. The acute oral and dietary studies for small mammals showed no mortality occurring at the highest dose tested in both study types. The small mammal dietary study demonstrated significant decrease in body weight gain at the 229.6 mg ai/kg bw dose level. The multi-generation study demonstrated effects on the viability and the number (F2) of pups per litter (F1 and F2) and the pup body weight at daily dietary concentrations of greater than 6.3 mg ai/kg bw.

Since Flumioxazin 51WDG Herbicide is to be applied twice per year, the EECs are based on residues immediately following the second application at the maximum rate and the minimum interval between applications. Because exposure is dependent on the body weight of the organisms and the amount and type of food consumed, the screening level risk assessment for birds and mammals considers a set of generic body weights (20, 100, 1000 g for birds and 15, 35, 1000 g for mammals) and food preferences (100% small insects for insectivores, 100% fruits for frugivores, 100% grain and seeds for granivores and 100% leaves and leafy crop for herbivores; food items considered at the screening level provide the most conservative EEC for each food guild). Additionally, the acute toxicity endpoint is divided by an uncertainty factor of 10 to account for potential differences in species sensitivity as well as varying protection levels (e.g. community, population, individual).

The calculated screening level risk quotients for birds and mammals (Appendix I, Table 13) indicate that the level of concern was not exceeded for birds and mammals on an acute and chronic basis, except for small mammals on a reproductive basis. For 0.015, 0.035 and 1 kg mammals, the level of concern was exceeded, and as a result, a refined assessment was conducted.

In the refined assessment (Appendix I, Table 14 and Table 15), how the product is expected to be used in the field, application method, application timing, dissipation half-life and foraging behaviour of the non-target animals are discussed to further refine and identify the potential reproductive risk to mammals.

Pesticide specific foliar dissipation data were not available for flumioxazin. The default value of 35 days used in the screening level risk assessment is based on the highest reported value (36.9 days) for foliar dissipation of a variety of active ingredients reported by Willis and McDowell and is considered to be conservative. For the on-field assessment, a half-life of 10 days was used. This value is obtained from the same dataset (Willis and McDowell), with 93% of the foliar dissipation a half-life of 10 days is considered to be a reasonable estimate of typical foliar half-lives. The EEC and EDE calculations are shown in Appendix I, Table 14. Risk quotients calculated for on-field exposure exceeded the level of concern for the reproductive endpoint of all food guilds and mammals size combinations. Where the level of concern was exceeded, refinement of the on-field scenario and an off-field assessment was conducted (Appendix I, Table 15).

For small herbivorous and frugivorus mammals, the on-field LOC is not expected to be exceeded since these food items are not expected to contain flumioxazin residues or be available for consumption on the field. Although risks were identified for insectivorous and granivorous mammals, it is expected that mammals will avoid feeding on open bare ground soil where they would be susceptible to predation when similar food items are available off-field under the cover of vegetation. It is therefore unlikely that the LOC for reproductive effects for wild mammals will be exceeded in the field under typical use conditions.

The off-field scenario assesses the risk to mammals that may be exposed to spray drift in habitats adjacent to the treated field. The off-field environmental concentration (EEC) was calculated based on the percent deposition at one metre downwind according to the ground application model used in the PMRA environmental assessments. This model predicts the percent deposition at one metre to be 6 % for applications using a ground boom sprayer and a medium spray quality.

An off-field assessment was conducted taking into consideration the spray drift deposition for medium sized spray droplets for ground application (6%). The LOC for reproductive effects was not exceeded for insectivorous, granivorous and frugivorous mammals of all weight categories. The reproduction level of concern was slightly exceeded for small herbivorous mammals of approximately 35 g and 1 kg body weight feeding on a diet of 100% short grass, forage crops or leafy foliage. Both the on-field and off-field assessment assumes maximum exposure concentration on food items immediately after application, that the concentration remains at these high levels and that mammals would feed exclusively on treated food within 1 m of the treated field and that the application timing coincides with the sensitive gestational period. Given that flumioxazin is expected to dissipate quickly in the environment, that it is unlikely that a small mammal would eat exclusively grass, forage crops and leafy foliage within 1 m of the treated field and that it is unlikely that the timing of application would always coincide with the sensitive gestation period, the refined assessment is representative of a conservative scenario. Although the RQ values indicate a small risk to small mammals, this risk is not likely to manifest itself in the field. Therefore, the reproductive risk to small mammals is not expected to manifest itself in the field.

Terrestrial Plants

Non-target terrestrial vascular plants could be exposed to residues of flumioxazin as a result of spray drift from the application of Flumioxazin 51WDG. Seedling emergence and vegetative vigour studies on ten crop species were submitted. Terrestrial plants were sensitive to flumioxazin with the most sensitive endpoints being EC_{25} value of 0.90 g a.i./ha and 0.09 g a.i./ha for seedling emergence and vegetative vigour, respectively. The maximum seasonal application rate considered for this assessment was 2 x 214 g ai/ha. The RQ determined indicates that the level of concern was exceeded for terrestrial plants (Appendix I, Table 16).

Given the conservative assumptions taken in the screening level assessment, a refined assessment was conducted to further characterize the risk by taking into consideration the dissipation half-lives of flumioxazin in the environment and an off-field exposure resulting from pesticide drift during application (Appendix I, Table 17). The application rate (or the rate at which the non-target plants will be exposed) was determined taking into consideration the

percent drift that will result depending on the application method. A spray droplet size of 'medium' based on the American Society of Agricultural Engineers (ASAE) classification can be assumed for herbicides applied by field sprayer. For a 'medium' droplet size, the maximum spray drift deposition for ground boom sprayer to agricultural crops at one metre downwind from the point of application is 6% of the application rate. The maximum percent off-field deposition on non-target plants would therefore be 14.45 g a.i./ha (2 x 214 g a.i./ha assuming 6% drift and a 10-day foliar half-life for vegetative vigour and a 111 day soil half-life for seedling emergence). Risk quotients calculated for the off-field exposure exceeded the level of concern. Where the level of concern was exceeded, a further refinement examining the toxicity endpoints used in the on-field scenario and an off-field assessment was conducted (Appendix I, Table 18).

An additional refinement step was conducted to further characterize on-field and off-field risk by taking into consideration non-crop plant toxicity data and an off-field exposure resulting from pesticide drift during application (Appendix I, Table 18). For this assessment, the HC_5 (hazard concentration at the 5th percentile) of the EC_{50} for the non-crop plant toxicity data was used as the toxicity value. The HC_5 of the EC_{50} values for all crops was determined to be 0.2732 g a.i./ha. Based on the revised RQs using the off-field EECs from drift and the non-crop plant toxicity information, the level of concern for terrestrial vascular plants was still exceeded.

The use of Flumioxazin 51WDG Herbicide may pose risks to non-target terrestrial plants. These risks may be mitigated by applying spray buffer zones and label statements.

4.2.2 Effects on Aquatic Organisms

Risk of flumioxazin and its related end-use products to freshwater aquatic organisms was based upon the evaluation of toxicity data for the following (Appendix 1, Table 11):

- One invertebrate species; daphnid (acute and long-term exposure);
- Two fish species (acute and stage specific exposure);
- One green algae, one blue-green algae, one diatom and one vascular plant; and
- Amphibian species using fish toxicity studies as surrogate.

Risk of flumioxazin to marine aquatic organisms was based upon evaluation of toxicity data for the following (Appendix 1, Table 11):

- Two invertebrates; mysid and eastern oyster (acute exposure);
- One fish species (acute exposure); and
- One diatom.

Aquatic organisms can be exposed to flumioxazin as a result of drift and runoff from the application of Flumioxazin 51WDG Herbicide. To assess the potential effects from exposure to flumioxazin, the screening level EECs in the aquatic environment based on direct application to water were used as exposure estimates. The calculated EECs were those determined in 15 cm body of water for amphibians and 80 cm body of water for all other aquatic organisms. For the screening level risk assessment for aquatic organisms the laboratory endpoints were adjusted using uncertainty factors to account for differences in species sensitivity and protection goals (e.g. community, population and individual).

In those cases where the screening level assessments resulted in the LOC being exceeded, a refined assessment was conducted to further characterize the risk. Given the conservative assumptions in the screening level assessment which assumes a direct overspray to a water body, a refined assessment was conducted to further characterize the identified risk from drift and runoff to freshwater and marine organisms (Appendix I, Table 21).

For drift, a refined EEC for a ground broadcast application was calculated using a maximum percent drift deposition at one metre downwind of the site of application. A spray droplet size of 'medium' based on the ASAE classification can be assumed for herbicides applied by field sprayer. For a 'medium' droplet size, the maximum spray drift deposition for ground boom sprayer to agricultural crops at one metre downwind from the point of application is 6% of the application rate.

For runoff, a refined EEC using the maximum application rate for flumioxazin on a body of water that is 1 hectare in area and is either 15-cm (amphibians) or 80-cm (all other aquatic organisms) deep was estimated by PRZM-EXAMS. The EECs used for the RQ calculations were the most conservative estimates for a particular time interval representative of the exposure period of the toxicity test.

Aquatic Invertebrates – Freshwater and Marine

The acute toxicity studies with flumioxazin using daphnids demonstrated mortality/immobility with a 48-h EC_{50} of 5.9 mg ai/L. The acute toxicity for flumioxazin to marine invertebrates demonstrated a 96-h LC_{50} of 0.23 mg ai/L. Shell deposition for marine mollusk was affected at an EC_{50} of 2.8 mg ai/L. Reproductive effects on daphnids and mysid shrimp were noted for flumioxazin with a NOEC of 0.050 mg ai/L (reproduction and survivability) and 0.0015 mg a.i./L (reproduction and growth), respectively. Calculated risk quotients for both freshwater and marine invertebrates demonstrate that the LOC for acute effects was not exceeded (Appendix I, Table 19). The LOC was exceeded, however, for reproductive effects on daphnids and mysid shrimp (Appendix I, Table 19). A refined assessment for these effects was therefore conducted.

Given the conservative assumptions in the screening level assessment which assumes a direct overspray to a water body, a refined assessment was conducted to further characterize the reproductive risk from drift and runoff to freshwater and marine invertebrates (Appendix I, Table 20 and Table 21). Based on the revised RQs using the off-field EECs from run-off concentrations estimated from PRZM/EXAMS modeling and the chronic invertebrate toxicity information, the level of concern for freshwater invertebrates was not exceeded. Based on the revised RQs using the off-field EECs from drift and the chronic invertebrate toxicity

information, the level of concern for freshwater invertebrates was not exceeded. The level of concern was, however, slightly exceeded for marine invertebrates using the off-field EECs from drift. These risks may be mitigated by applying spray buffer zones and label statements.

Fish – Freshwater and Marine

Acute toxicity studies with flumioxazin were submitted for two freshwater fish and one marine fish species. A chronic early life stage toxicity study for rainbow trout was also submitted. The acute toxicity studies with flumioxazin using rainbow trout and bluegill sunfish demonstrated mortality with 96-h EC_{50} values of 2.3 mg a.i./L and >21 mg a.i./L, respectively. Chronic effects were noted on reduced body length and reduced weight with a NOEC of 7.7 µg a.i./L. Calculated risk quotients for both freshwater and marine fish indicate that the LOC for acute effects was not exceeded (Appendix I, Table 19). The LOC was exceeded, however, for chronic effects on rainbow trout (Appendix I, Table 19). A refined assessment for these effects was therefore conducted.

Given the conservative assumptions in the screening level assessment which assumes a direct overspray to a water body, a refined assessment was conducted to further characterize the reproductive risk from drift and runoff to fish on a chronic basis (Appendix I, Table 20 and Table 21). Based on the revised RQs using the off-field EECs from drift and runoff concentrations estimated from PRZM/EXAMS modeling and the chronic fish toxicity information, the level of concern was not exceeded. Therefore, chronic adverse effects on fish populations as a result of the application of flumioxazin are not expected.

Amphibians

No studies assessing the toxicity of flumioxazin to amphibians were submitted. In order to assess the risk to amphibians resulting from an acute and a chronic exposure to flumioxazin, the endpoint values for the most sensitive fish species were used as surrogate data, along with the EEC in a 15-cm deep body of water. The acute toxicity study with flumioxazin using rainbow trout demonstrated mortality with 96-h EC_{50} values of 2.3 mg a.i./L. Chronic effects were noted on reduced body length and reduced weight at a NOEC of 7.7 µg a.i./L. Calculated risk quotients for amphibians indicate that the LOC for acute and chronic effects was exceeded (Appendix I, Table 19). A refined assessment for these effects was therefore conducted.

Given the conservative assumptions in the screening level assessment which assumes a direct overspray to a water body, a refined assessment was conducted to further characterize the risk from drift and runoff to amphibians on an acute and chronic basis (Appendix I, Table 20 and Table 21). Based on the revised RQs using the off-field EECs from drift and runoff concentrations estimated from PRZM/EXAMS modeling and the acute and chronic fish toxicity information, the LOC was only exceeded from exposure to drift. These risks may be mitigated by applying spray buffer zones and label statements.

Aquatic Plants
Acute studies of freshwater algae and vascular plant exposure to flumioxazin were submitted. The most sensitive endpoints determined for acute exposure were EC_{50}: 8.3µg a.i./L and 0.33 µg a.i./L for flumioxazin to algae and vascular plants, respectively. The calculated risk quotients indicate that the RQ for acute exposure of aquatic plants exceeds the LOC (Appendix I, Table 19).

Given the conservative assumptions in the screening level assessment which assumes a direct overspray to a water body, a refined assessment was conducted to further characterize the acute risk from drift and runoff to algae and vascular plants (Appendix I, Table 20 and Table 21). Based on the revised RQs using the off-field EECs from drift and runoff concentrations estimated from PRZM/EXAMS modeling and the acute aquatic plant toxicity information, the LOC was still exceeded.

The modeled exposure output for runoff was further analysed to characterise the risk estimate to the most sensitive organism tested, duckweed. Analysis of the PRZM-EXAMS 96-h time-weighted yearly peak concentrations for the most conservative scenario showed that there is a 60% probability of exceeding the LOC in a given year based on the current toxicity endpoints. This estimate is derived directly from the model output, showing that the endpoint of concern of 0.165 µg total residues (TR)/L is exceeded in 87% of years based on a 50-year meteorological input file for Flumioxazin 51WDG Herbicide (Appendix I, Table 22). Therefore, runoff and drift are both expected to pose a risk to freshwater algae and vascular plants. These results should be considered preliminary since there is uncertainty associated with both the toxicity study results and the environmental exposure estimate from runoff. Flumioxazin is a contact herbicide and is, therefore, expected to elicit a different toxic response if plants and algae are exposed via drift or direct overspray. An additional overspray study is required to address the uncertainties and to characterise the risk from drift and overspray to aquatic plants.

The risks identified from drift may be mitigated by applying spray buffer zones and label statements. Advisory runoff statements on the label may minimize the risk from runoff to aquatic plants.

4.2.3 Granular Application

Flumioxazin 0.25G Herbicide
Flumioxazin 0.25G Herbicide is a granular formulation to be applied to outdoor container-grown ornamentals. Flumioxazin, when applied as the 0.25G formulation, is not expected to move through the environment via drift. Container-grown ornamentals are kept on different types of soil to facilitate the movement of excess water away from the containers. These containers may be kept on well-drained soil, such as gravel and coarse-textured soils, to assist the vertical movement of water away from the containers or on a soil promoting the horizontal movement of excess water away from the containers. The aquatic environment may be exposed from both types of systems. In well-drained soil, particularly if a tile drainage system is in place, exposure of the aquatic environment may occur through leaching and/or effluent discharge through the tile drainage system. In fields designed to assist the horizontal movement of excess water, aquatic

systems may be exposed through runoff. Since Flumioxazin 0.25G Herbicide is a granular pesticide, exposure through drift is not expected and drift was not included in the refined assessment.

In the terrestrial environment, Flumioxazin 0.25G Herbicide, at the proposed application rate is not expected to pose a risk to earthworms, bees, beneficial arthropods and birds (Appendix 1, Table 23 and 24). Exposure to non-target terrestrial plants, bees and beneficial arthropods is expected to be minimal since spray drift is not expected to result from the application of a granular based pesticide and the RQ values indicate that the level of concern is not expected to be exceeded for earthworms and birds. A risk to small mammals was identified, however, nurseries may already have measures in place to control for rodents and the application instructions require that the treatment area is irrigated immediately after treatment, thereby dissolving the granules. Therefore, exposure of small mammals to Flumioxazin 0.25G Herbicides granules is unlikely. Flumioxazin 0.25G Herbicide is not expected to pose a risk to terrestrial organisms.

To assess the potential for effects from exposure to flumioxazin, screening level EECs in the aquatic environment based on a direct application to water were used as the exposure estimates at the maximum proposed application rate (two applications of 420 g a.i./ha). The calculated risk quotients for exposure indicate that the LOC is exceeded for algae, amphibians and diatoms on an acute basis and daphnids, fish, amphibians and mysid shrimp on a chronic basis (Appendix I, Table 25).

Given the conservative assumptions in the screening level assessment which assumes a direct overspray to a water body, a refined assessment was conducted to further characterize the identified risk from runoff to freshwater and marine organisms (Appendix I, Table 26).
For runoff, a refined EEC using the maximum application rate for flumioxazin on a body of water that is 1 hectare in area and is either 15-cm (amphibians) or 80-cm (all other aquatic organisms) deep was estimated by PRZM-EXAMS. The EECs used for the RQ calculations were the 90th percentile estimates for a particular time interval representative of the exposure period of the toxicity test. Based on the revised RQs using the off-field EECs from runoff and the acute aquatic plant toxicity information, the LOC was still exceeded.

The modeled exposure output for runoff was further analysed to refine the risk estimate to the most sensitive organisms tested, duckweed. Analysis of the PRZM-EXAMS 96-h time-weighted yearly peak concentrations for the most conservative scenario showed that there is a 100% probability of exceeding the LOC in a given year based on the current toxicity endpoint. This estimate is derived directly from the model output, showing that the endpoint of concern of 0.165 µg total residues (TR)/L is exceeded every year based on a 50-year meteorological input file for Flumioxazin 0.25G Herbicide (Appendix I, Table 27). These results should be considered preliminary since there is a significant amount of uncertainty in both the toxicity study results and the environmental exposure estimate from runoff. An additional overspray study is required to address the uncertainties and to characterise the risk to aquatic plants.

In the aquatic environment, Flumioxazin 0.25G Herbicide, at the proposed application rate is not expected to pose a risk to aquatic invertebrates, fish and amphibians on an acute or chronic basis. Flumioxazin 0.25G Herbicide may pose a risk to algae and vascular plants on an acute basis if runoff containing flumioxazin is discharged into water bodies. Advisory runoff statements on the label may minimize the risk from runoff to aquatic plants.

5.0 Value

5.1 Flumioxazin 51WDG Herbicide

5.1.1 Effectiveness of Flumioxazin 51WDG Herbicide Against Pests

Efficacy data for flumioxazin applied alone were submitted from 77 replicated field trials conducted between 1990 and 2008 at several locations in British Columbia, Manitoba, Ontario, Quebec, Prince Edward Island, Oregon, Washington, Idaho, North Dakota, Minnesota, Wisconsin, and Michigan. An additional 41 trials conducted in non-border US states (California, Colorado, Illinois, Connecticut, Pennsylvania, New Jersey, Virginia, North Carolina, Louisiana, and Mississippi) were included in the review as supplementary information. Efficacy data were examined at various rates to determine the lowest effective rate. The herbicide treatments were applied using small plot application equipment.

5.1.1.1 Acceptable Efficacy Claims for Flumioxazin 51WDG Herbicide

Based on the efficacy data provided, the lowest effective rate for Flumioxazin 51WDG Herbicide was established for coarse-textured soils with less than 5% OM, medium-textured soils with less than 5% OM and muck soils. The established rates and supported weed claims are summarized in Table 5.1.1.1.1.

Table 5.1.1.1.1 Weed Control Claims for Flumioxazin 51WDG Herbicide

Soil Conditions	Herbicide Rate	Weeds Controlled
Coarse-textured soils < 5% OM	71 or 140 g a.i./ha	**Control:** common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, dandelion
Medium-textured soils < 5% OM	107 or 214 g a.i./ha	
Coarse- and medium-textured soils < 5% OM	54 g a.i./ha	**Suppression:** common lamb's-quarters, redroot pigweed, eastern black nightshade, hairy nightshade
Muck soils	71 g a.i./ha	**Suppression:** common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade
Do not apply on mineral soils with > 5% OM, or on fine-textured soils.		

5.1.1.2 Herbicide Tank Mix Combinations for Flumioxazin 51WDG Herbicide

Adequate data were provided to support the proposed herbicide tank mixture of Flumioxazin 51WDG Herbicide with glyphosate present as the isopropylamine salt (e.g. Roundup Original, Roundup Transorb, Roundup WeatherMax). No reduction in weed control was observed when Flumioxazin 51WDG Herbicide was tank-mixed with glyphosate.

5.1.2 Phytotoxicity of Flumioxazin 51WDG Herbicide to Host Plants

Data from 210 trials (28 trials on soybean, 28 trials on ornamental trees, 14 trials on dry-bulb onion, 13 trials on apple, 23 trials on pear, 14 trials on grape, 12 trials on asparagus, 6 trials on highbush blueberry, 12 trials on peach, 20 trials on cherry, 2 trials on nectarine, 7 trials on plum, 11 trials on potato, and 20 trials on strawberry) were provided in support of the host crop tolerance claims. Some trials included multiple crops. Trials were conducted at multiple locations from 1989 to 2006 in British Columbia, Manitoba, Ontario, Quebec, Nova Scotia, Prince Edward Island, Oregon, Washington, North Dakota, Minnesota, Wisconsin, Michigan, Illinois, California, Connecticut, Pennsylvania, New York, New Jersey, Virginia, North Carolina, Mississippi, and Georgia.

5.1.2.1 Acceptable Claims for Host Plant

Crop injury and crop yield data with Flumioxazin 51WDG Herbicide applied alone or in tank-mixture support a crop tolerance claim for soybean, ornamental trees, dry-bulb onion, apple, pear, grape, asparagus, highbush blueberry, peach, cherry, nectarine, plum, apricot potato and strawberry. In the case of strawberry, the data submitted provided variable results in terms of crop tolerance, therefore, appropriate warning statements will be required on the product label.

5.1.3 Impact of Flumioxazin 51WDG on Succeeding Crops

The submitted crop injury and yield data support a rotational crop tolerance claim for the following after an application of Flumioxazin 51WDG Herbicide (recrop intervals are indicated in brackets): soybean (immediate), winter wheat (4 months), spring wheat (8 months), field corn (9 months), sunflower (9 months), sorghum (9 months), dry common beans (9 months), canola (9-11 months), alfalfa (11 months), and barley (11 months).

5.1.4 Economics of Flumioxazin 51WDG Herbicide

The Flumioxazin 51WDG Herbicide label includes many minor use crops, many of which have limited options for weed control, especially for pre-emergence weed control. Flumioxazin 51WDG Herbicide has been identified as a National Minor Use Priority, through Agriculture and Agri-Food Canada's Pest Management Centre (AAFC-PMC), for weed control in dry-bulb onion, ornamentals, apple, grape, potato and strawberry. The registration of Flumioxazin 51WDG Herbicide will provide Canadian growers access to a herbicide technology currently available to growers from other countries. This allows Canadian growers to compete on a more equal level in foreign and domestic markets.

5.1.5 Sustainability of Flumioxazin 51WDG Herbicide

5.1.5.1 Survey of Alternatives

Bare ground non-crop areas
Several currently registered products provide post-emergence control of weeds in non-crop areas (group 4, group 2, or group 11). However, only 2 other products are registered for pre-emergence weed control in non-crop areas (Table 5.1.5.1.1). Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for weed control in non-crop areas.

Table 5.1.5.1.1 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in non-crop areas

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
bromacil	Hyvar	5	no weed list
diuron	Karmex	7	Annual and perennial grasses and broadleaf weeds

Field-grown ornamentals (deciduous or coniferous)
Several products are currently registered for post-emergence weed control in ornamentals (list not shown). Examples of pre-emergence herbicides for use in ornamentals are listed in Table 5.1.5.1.2. Only one other group 14 herbicide provide pre-emergence weed control in ornamentals, Ronstar (oxadiazon). However, this product can only be used in container-grown ornamentals.

Table 5.1.5.1.2 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in ornamentals.

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
chlorthal	Dacthal	3	annual grasses and broadleaf weeds
dichlobenil	Casoron	20	annual grasses and broadleaf weeds
napropamide	Devrinol	15	annual grasses and broadleaf weeds
oxadiazon	Ronstar	14	annual grasses and broadleaf weeds
simazine	Simazine, Simadex, Princep Nine-T	5	annual grasses and broadleaf weeds
trifluralin	Treflan, Rival, Bonanza	3	annual grasses and broadleaf weeds

Soybean

Several products are currently registered for pre-plant or pre-emergence weed control in soybean. Examples are listed in Table 5.1.5.1.3. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for weed control in soybean.

Table 5.1.5.1.3 Alternative herbicides that provide pre-plant or pre-emergence weed control (applied pre-emergence to weeds) in soybean

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
flufenacet/metribuzin	Axiom	5 & 15	annual grasses and broadleaf weeds
Imazethapyr	Pursuit	2	annual grasses and broadleaf weeds
Metribuzin	Sencor	5	annual grasses and broadleaf weeds
Linuron	Lorox	7	annual grasses and broadleaf weeds
flumetsulam/s-metolachlor	Broadstrike Dual Magnum	2 & 15	annual grasses and broadleaf weeds
cloransulam-methyl	FirstRate	2	annual broadleaf weeds
s-metolachlor/benoxcor	Dual II Magnum	15	annual grasses and broadleaf weeds
s-metolachlor/metribuzin	Boundary	5	annual grasses and broadleaf weeds
Dimethenamid	Frontier	15	annual grasses and broadleaf weeds
Trifluralin	Treflan, Rival, Bonanza	3	annual grasses and broadleaf weeds
imazethapyr/pendimethalin	Valor	2 & 3	annual grasses and broadleaf weeds

Dry-bulb onion

Several registered products (not listed) provide post-emergence weed control (post to weeds) in dry-bulb onion. Few products are currently registered for pre-emergence weed control (pre-emergence to weeds) in dry-bulb onion. These herbicides are listed in Table 5.1.5.1.4. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for pre-emergence weed control in dry-bulb onion.

Table 5.1.5.1.4 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in dry-bulb onion.

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
Pendimethalin	Prowl 400 EC Herbicide	3	annual grasses and broadleaf weeds
Dimethenamid	Frontier Herbicide	15	suppression of yellow nutsedge
chlorthal	Dacthal W-75 Herbicide	3	annual grasses and broadleaf weeds

Pome fruit (apple and pear)

Examples of pre-emergence herbicides for use in pome fruit (apple and pear) are listed in Table 5.1.5.1.5. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for pre-emergence weed control in pome fruit.

Table 5.1.5.1.5 lternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in pome fruit (apple and pear)

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
dichlobenil	Casoron	20	annual and perennial grasses and broadleaf weeds
napropamide	Devrinol	15	annual grasses and broadleaf weeds
linuron	Lorox	7	annual grasses and broadleaf weeds
s-metolachlor/benoxacor	Dual II Magnum	15	annual grasses and broadleaf weeds
metribuzin	Sencor, Lexone	5	annual grasses and broadleaf weeds
propyzamide	Kerb	15	annual grasses, perennial grasses and chickweed
terbacil	Sinbar	5	annual grasses and broadleaf weeds
simazine	Simazine, Simadex, Princep Nine-T	5	annual grasses and broadleaf weeds
trifluralin	Treflan, Bonanza	3	annual grasses and broadleaf weeds

Grape

Examples of pre-emergence herbicides for use in grape are listed in Table 5.1.5.1.6. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for pre-emergence weed control in grape.

Table 5.1.5.1.6 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in grape.

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
dichlobenil	Casoron	20	annual and perennial grasses and broadleaf weeds
napropamide	Devrinol	15	annual grasses and broadleaf weeds
diuron	Karmex	7	annual grasses and broadleaf weeds
dimethenamid	Frontier	15	annual grasses and broadleaf weeds
simazine	Simazine, Simadex, Princep Nine-T	5	annual grasses and broadleaf weeds

Highbush blueberry

Examples of pre-emergence herbicides for use in highbush blueberry are listed in Table 5.1.5.1.7. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for pre-emergence weed control in highbush blueberry.

Table 5.1.5.1.7 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in highbush blueberry

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
dichlobenil	Casoron	20	annual and perennial grasses and broadleaf weeds
napropamide	Devrinol	15	annual grasses and broadleaf weeds
terbacil	Sinbar	5	annual and perennial grasses and broadleaf weeds
simazine	Simazine, Simadex, Princep Nine-T	5	annual grasses and broadleaf weeds

Stone fruit

Examples of pre-emergence herbicides for use in stone fruit (peach, cherry, nectarine, plum, and apricot) are listed in Table 5.1.5.1.8. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for pre-emergence weed control in stone fruit.

Table 5.1.5.1.8 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in stone fruit (peach, cherry, nectarine, plum, and apricot)

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
Dichlobenil	Casoron	20	annual and perennial grasses and broadleaf weeds
Napropamide	Devrinol	15	annual grasses and broadleaf weeds
s-metolachlor/benoxacor	Dual II Magnum	15	annual grasses and broadleaf weeds
Metribuzin	Sencor, Lexone	5	annual grasses and broadleaf weeds
Terbacil	Sinbar	5	annual grasses and broadleaf weeds
Simazine	Simazine, Simadex, Princep Nine-T	5	annual grasses and broadleaf weeds
Trifluralin	Treflan, Bonanza	3	annual grasses and broadleaf weeds

Asparagus

Examples of pre-emergence herbicides for use in asparagus are listed in Table 5.1.5.1.9. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for pre-emergence weed control in asparagus.

Table 5.1.5.1.9 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in asparagus

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
Napropamide	Devrinol	15	annual grasses and broadleaf weeds
Terbacil	Sinbar	5	annual grasses and broadleaf weeds

Potato

Examples of pre-emergence herbicides for use in potato are listed in Table 5.1.5.1.10. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for pre-emergence weed control in potato.

Table 5.1.5.1.10 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in potato.

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
linuron	Lorox, Afolan, Linuron	7	annual grasses and broadleaf weeds
s-metolachlor	Dual Magnum, Dual II Magnum	15	annual grasses and broadleaf weeds
metribuzin	Sencor, Lexone	5	annual grasses and broadleaf weeds

Strawberry

Examples of pre-emergence herbicides for use in strawberry are listed in Table 5.1.5.1.11. Flumioxazin 51WDG Herbicide is a group 14 herbicide and represents a new mode of action for pre-emergence weed control in strawberry.

Table 5.1.5.1.11 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in strawberry.

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
terbacil	Sinbar	5	annual grasses and broadleaf weeds
napropamide	Devrinol	15	annual grasses and broadleaf weeds
s-metolachlor	Dual Magnum, Dual II Magnum	15	annual grasses and broadleaf weeds

5.1.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

The registration of Flumioxazin 51WDG Herbicide is compatible with current management practices, including IPM, for all proposed crops. Flumioxazin 51WDG Herbicide has no negative impact on beneficial insects or microbes, due to its mode of action.

5.1.5.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

With the exception of ornamentals, Flumioxazin 51WDG Herbicide (group 14 herbicide) represents a new mode of action for pre-emergence weed control. Therefore, flumioxazin will provide a key tool in resistance management.

5.2 Flumioxazin 0.25G Herbicide

5.2.1 Effectiveness of Flumioxazin 0.25G Herbicide Against Pests

Efficacy data for flumioxazin applied alone were submitted from 13 replicated field trials conducted between 2005 and 2006 at several locations in British Columbia, Alberta, Ontario, and Quebec. Efficacy data were examined at various rates to determine the lowest effective rate. The herbicide treatments were applied using hand-held shakers to container-grown ornamentals.

5.2.1.1 Acceptable Efficacy Claims for Flumioxazin 0.25G Herbicide

Based on the efficacy data provided, the lowest effective rate for Flumioxazin 0.25G Herbicide was established as 210 g a.i./ha or 420 g a.i./ha, with the rate varying with weed claims. The established rates and supported weed claims are summarized in Table 5.2.1.1.1.

Table 5.2.1.1.1 Weed Control Claims for Flumioxazin 0.25G Herbicide

Herbicide Rate	Weeds Controlled
210 g a.i./ha	**control:** hairy bittercress/snapweed
420 g a.i./ha	weeds listed above plus **control:** liverwort **suppression:** common groundsel, common chickweed

5.2.1.2 Herbicide Tank Mix Combinations for Flumioxazin 0.25G Herbicide

None.

5.2.2 Phytotoxicity of Flumioxazin 0.25G Herbicide to Host Plants

Data from 14 trials were provided in support of the host crop tolerance claims. Within each trial crop tolerance data were provided for 3-10 host species, for a total of 78 trial-host combinations. Trials were conducted at multiple locations from 2005 to 2006 in British Columbia, Alberta, and Ontario.

5.2.3 Impact of Flumioxazin 0.25G on Succeeding Crops

Not applicable.

5.2.4 Economics of Flumioxazin 0.25G Herbicide

Flumioxazin 0.25G Herbicide provides control or suppression of economically important weeds found in container-grown ornamentals. Containers must be kept weed free for marketability and to maintain healthy container stock.

5.2.5 Sustainability of Flumioxazin 0.25G Herbicide

5.2.5.1 Survey of Alternatives

Examples of pre-emergence herbicides for use in container-grown ornamentals are listed in Table 5.2.5.1.1. Only one other group 14 herbicide provides pre-emergence weed control in ornamentals, Ronstar (oxadiazon). However, according to the label, this product does not control liverwort, hairy bittercress/snapweed, or common chickweed, which are key weed species for controll in container-grown ornamentals. These weed species are listed on the Flumioxazin 0.25G Herbicide label.

Table 5.2.5.1.1 Alternative herbicides that provide pre-emergence weed control (applied pre-emergence to weeds) in ornamentals.

Active Ingredient	Product	Mode of Action Group #	Spectrum of Weed Control
Chlorthal	Dacthal	3	annual grasses and broadleaf weeds
Dichlobenil*	Casoron	20	annual grasses and broadleaf weeds
napropamide*	Devrinol	15	annual grasses and broadleaf weeds
Oxadiazon*	Ronstar	14	annual grasses and broadleaf weeds
Simazine*	Simazine, Simadex, Princep Nine-T	5	annual grasses and broadleaf weeds
Trifluralin	Treflan, Rival, Bonanza	3	annual grasses and broadleaf weeds

*: specifically for container-grown ornamentals

5.2.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

The registration of Flumioxazin 0.25G Herbicide is compatible with current management practices, including IPM, for all proposed crops. Flumioxazin 0.25G Herbicide has no negative impact on beneficial insects or microbes, due to its mode of action.

5.2.5.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Flumioxazin 0.25G Herbicide represents a relatively new mode of action (group 14) for herbicides in container-grown ornamentals. Therefore rotation with traditional products such as Casoron (group 20) and Devrinol (group 15) should delay the occurrence of herbicide resistance.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that meet all four criteria outlined in the policy, i.e., CEPA-toxic or equivalent, predominantly anthropogenic, persistent and bio-accumulative).

During the review process, flumioxazin and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[4] and evaluated against the Track 1 criteria (see Table 28). The PMRA has reached the following conclusions:

- Flumioxazin does not meet Track 1 criteria, and is not considered a Track 1 substance. See Table 28 in Appendix I for comparison with Track 1 criteria.

- Limited information was provided on the chemistry and fate of the flumioxazin transformation products. The laboratory studies indicated that several major transformation products (482-HA, APF, THPA, HPA, SAT-482-HA, SAT-482-HA-2, DAPF) accumulate under hydrolysis and anaerobic aquatic conditions. Log K_{OW} information is required to determine whether they meet the TSMP criteria for bioaccumulation. If a predicted K_{OW} value is provided, a similar prediction with the parent compound should also be provided so that the PMRA can compare the predicted with the empirical value.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[5]. The list is used as described in the PMRA Notice of Intent NOI2005-01[6] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[7], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Technical grade flumioxazin and the end-use products Flumioxazin 51WDG Herbicide and Flumioxazin 0.25G Herbicide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

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4 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

5 *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

6 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

7 DIR2006-02, PMRA Formulants Policy.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for flumioxazin is adequate to define the majority of toxic effects that may result from exposure. In subchronic and chronic studies on laboratory animals, target organs included the blood system and the liver. There was no evidence of oncogenicity. Both qualitative and quantitative sensitivity of the young were observed in terms of fetal malformations at maternally non-toxic doses. Flumioxazin is not considered to be a neurotoxicant. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

The nature of the residue in plants (soybean, peanut, grape and apple) and animals (hen and goat) is adequately understood. The residue definition for enforcement purposes in plant products is flumioxazin. The use of flumioxazin on crops listed on the labels and the import of flumioxazin-treated commodities does not constitute an unacceptable chronic dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health. The PMRA recommends that the following maximum residue limits be specified for residues of flumioxazin.

MRLs (ppm)	Foods
0.02	Tuberous and Corm Vegetables (Crop Subgroup 1C); Bulb Onion Subgroup (Crop Subgroup 3-07A); Soybean, seed; Pome fruits (Crop Group 11), Stone fruits (Crop Group 12); Bushberries, except lowbush blueberries (Crop Subgroup 13-07B); Small fruit vine climbing, except fuzzy kiwifruit (Crop Subgroup 13-07F); asparagus
0.07	Low growing berries (Crop Subgroup 13-07G)

Mixer, loader applicators handling Flumioxazin 51WDG Herbicide or Flumioxazin 0.25G Herbicide and workers re-entering treated agricultural or ornamental crops, or bare ground non-crop areas are not expected to be exposed to levels of flumioxazin that will result in an unacceptable risk when Flumioxazin 51WDG Herbicide or Flumioxazin 0.25G Herbicide is used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

Health risks to bystanders are considered not to be of concern.

Health risks for people who enter treated fields to pick apples, pears, highbush blueberries, or strawberries are not of concern.

7.2 Environmental Risk

The use of Flumioxazin 51WDG Herbicide may pose a risk to terrestrial and aquatic organisms, including beneficial arthropods, terrestrial non-target vascular plants, algae and aquatic vascular plants. Precautionary label statements appear on the product labels to identify and mitigate the risk from spray drift to beneficial arthropods. Also, terrestrial spray buffer zones of five to thirty metres and aquatic buffer zones of one to five metres are required to protect sensitive non-target plant species from spray drift. Advisory runoff statements on the label may minimize the risk from runoff.

The use of Flumioxazin 0.25G Herbicide is not expected to pose a risk to terrestrial organisms when used according to the label directions. In the aquatic environment, Flumioxazin 0.25G at the proposed application rate is not expected to pose a risk to aquatic invertebrates, fish and amphibians on an acute or chronic basis. Flumioxazin 0.25G Herbicide may pose a risk to algae and vascular plants on an acute basis if runoff containing flumioxazin is discharged into water bodies. Advisory runoff statements on the label may minimize the risk from runoff to aquatic plants.

7.3 Value

The data submitted to register Flumioxazin 51WDG Herbicide are adequate to describe its efficacy for use in non-crop areas, field-grown coniferous ornamental trees, field-grown deciduous ornamental trees, soybean, dry-bulb onion, pome fruit (apple and pear), grape, highbush blueberry, stone fruit (peach, cherry, nectarine, plum, and apricot), asparagus, potato and strawberry. A single pre-emergence application of Flumioxazin 51WDG Herbicide provides control or suppression of common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, and dandelion. With the exception of strawberry, the submitted phytotoxicity and yield data demonstrate an adequate margin of safety of labelled host crops to Flumioxazin 51WDG Herbicide. The risk of crop injury to strawberry is mitigated through the use of warning statements on the product label. With the exception of ornamentals, Flumioxazin 51WDG Herbicide (group 14) provides a new mode of action for pre-emergence weed control for labelled crops.

7.3.2 Flumioxazin 0.25G Herbicide

The data submitted to register Flumioxazin 0.25G Herbicide are adequate to describe its efficacy for use in container-grown woody ornamentals. A single pre-emergence application of Flumioxazin 0.25G Herbicide provides control of hairy bittercress and liverwort and suppression of common groundsel and common chickweed. The submitted data demonstrate an adequate margin of safety of labelled woody ornamentals to Flumioxazin 0.25G Herbicide. Flumioxazin 0.25G Herbicide provides a relatively new mode of action (group 14) for herbicides in container-grown woody ornamentals.

7.4 Unsupported Uses

7.4.1 Flumioxazin 51WDG Herbicide

Certain uses originally proposed by the applicant were not supported by the PMRA because the value was not adequately demonstrated. These uses include:

- 37 weed claims (see Appendix I, Table 29) and
- some ornamental species and sweet potato (see Appendix I, Table 30).

7.4.2 Flumioxazin 0.25G Herbicide

Certain uses originally proposed by the applicant were not supported by the PMRA because the value was not adequately demonstrated. These uses include:

- 42 weed claims (see Appendix I, Table 31) and
- some ornamental species (see Appendix I, Table 32).

8.0 Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for the sale and use of Flumioxazin Technical, Flumioxazin 51 WDG to control weeds in several crops and Flumioxazin 0.25 G to control weeds in container grown ornamentals.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

Although the risks and value have been found acceptable when all risk-reduction measures are followed, as a condition of these registrations, additional scientific information is being requested from the applicant. For more details, refer to the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information to the PMRA by September 30, 2012.

Environment

- The $\log K_{OW}$ is required for the major transformation products identified in the aquatic environment;

- An analytical method for the analysis of the major transformation products in aquatic systems is required:

- Either one of the following two studies is required: an aerobic water biotransformation study, or an aerobic water/sediment biotransformation study;

- Ecotoxicology studies on daphnids, rainbow trout and aquatic vascular plants conducted with transformation products expected to accumulate in the aquatic environment are conditionally required, pending the results of the aerobic aquatic biotransformation study;

- An overspray study is required to characterise the risk from drift and overspray to aquatic plants.

Chemistry

- Analytical data from at least five batches of TGAI representing full-scale production.

- Mass spectra or chromatograms confirming identity of active ingredient and impurities.

- Storage stability data for the EPs representing at least one year of storage at ambient conditions.

Value

For Flumioxazin 51WDG Herbicide:

- Five efficacy trials conducted on coarse-textured soils with less than 5% OM (organic matter) for each of the following seven weed species: redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, and dandelion.

- Five efficacy trials conducted on medium-textured soils with less than 5% OM for each of the following eight weed species: common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, and dandelion.

- Three to four efficacy trials conducted in potato for each of the following four weed species: common lamb's-quarters, redroot pigweed, eastern black nightshade, and hairy nightshade.

- Three to four efficacy trials conducted on muck soil for each of the following six weed species: common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, and hairy nightshade.

- Three soybean crop tolerance trials conducted on medium-textured soils with 3-5% OM.

- Three asparagus crop tolerance trials conducted on coarse-textured soils with < 5% OM and an additional three trials conducted on medium-textured soils with < 5% OM.

- Three crop tolerance trials conducted on apricot for both broadcast application to dormant trees and directed applications to vegetative trees.

- Three to four crop tolerance trials conducted on strawberry for both broadcast application to dormant plants, and hooded or shielded applications to row middles prior to fruit set.

- Two to three soybean rotational crop trials conducted on medium-textured soils with 3-5% OM.

NOTE: The PMRA will publish a consultation document at the time when there is a proposed decision on applications to convert these conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

List of Abbreviations

µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmosphere
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetres
DF	dry flowable
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in the test population)
DT_{75}	dissipation time 75% (the dose required to observe a 75% decline in the test population)
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
ER_{25}	effective rate for 25% of the population
g	gram
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
mg	milligram
mL	millilitre
MAS	maximum average score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NOAEL	no observed adverse effect level

NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
PBI	plantback interval
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RSD	relative standard deviation
SC	soluble concentrate
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Plant	RM-30A Enforcement Method	Flumioxazin	GC-NPD (gas chromatography with nitrogen phosphorus detector)	0.02 ppm	1442705 1442724
	RM-30A-1	Flumioxazin	GC-NPD	0.02 ppm	1288589 1288648
	RM-30A-3	Flumioxazin	GC-NPD GC-MSD (gas chromatography with mass selective detector)	0.02 ppm	1442682
	RM-30B	Flumioxazin	GC-NPD	0.02 ppm	1442705 1442724
	RM-30C	Flumioxazin	GC-NPD	0.02 ppm	1442705 1442724
	RM-30M	1-OH-HPA and its conjugates	GC-MSD	0.02 ppm	1442724
	RM-30P	1-OH-HPA and its conjugates	GC-MSD	0.02 ppm	1442724
Animal	RM-30MK	Flumioxazin 3-OH Flumioxazin 4-OH-flumioxazin	HPLC-MS/MS	0.02 ppm	1442755
	RM-30T	Flumioxazin 3-OH Flumioxazin 4-OH-flumioxazin	HPLC-MS/MS	0.02 ppm	1442755
Soil	RM-30S-1 RM-30S-2	Flumioxazin	GC/MS	0.02 ppm	1437732 143773
		metabolites			
Sediment		Same method as soil			
Water	ER-MT-9211	Flumioxazin	GC/FID	0.5 ppb	1437735

Table 2 Acute Toxicity of Flumioxazin and the Associated End-use Products Flumioxazin 0.25G Herbicide and Flumioxazin 51WDG Herbicide

Study Type	Species	Result	Comment
Acute Toxicity of Flumioxazin Technical			
Oral	Rat	LD_{50} > 5000 mg/kg bw	LOW TOXICITY
Dermal	Rat	LD_{50} > 2000 mg/kg bw	LOW TOXICITY
Inhalation	Rat	LC_{50} > 3.93 mg/L	LOW TOXICITY
Skin irritation	Rabbit	MAS[a] = 0	Non-irritating
Eye irritation	Rabbit	MAS = 0.4	Minimally irritating
Skin sensitization (Maximization)	Guinea pig	Negative	
Acute Toxicity of End-Use Products: Broadstar Herbicide, Valtera Herbicide, Chateau Herbicide WDG,			

Study Type	Species	Result	Comment
Sureguard Herbicide, Payload Herbicide, Flumioxazin 0.25G Herbicide, and Flumioxazin 51WDG Herbicide			
Oral	Rat	LD_{50} > 5000 mg/kg bw	LOW TOXICITY
Dermal	Rat	LD_{50} > 2000 mg/kg bw	LOW TOXICITY
Inhalation	Rat	LC_{50} > 0.969 mg/L	SLIGHT TOXICITY
Skin irritation	Rabbit	MAS = 0.3	Minimally irritating
Eye irritation	Rabbit	MAS = 1.2	Minimally irritating
Skin sensitization (Maximization)	Guinea pig	Negative	

[a] MAS = Maximum average score for 24, 28 and 72 hours

Table 3 Toxicity Profile of Technical Flumioxazin

Study Type	Species	Results[a] (mg/kg/day)
3-month dietary	Rat	NOAEL: 69.7 LOAEL: 229.6; decreased body weight gain, hematotoxicity, increased spleen weight
3-month dietary	Rat	NOAEL: 19.3 LOAEL: 65.0; hematotoxicity, mostly in females
3-month capsule	Dog	NOAEL: 100 LOAEL: 1000; increased liver weight, increased macro and microscopic liver pathology, loose feces
4-week dermal	Rat	NOAEL: 1000 LOAEL: Not determined
1-year capsule	Dog	NOAEL: 100 LOAEL: 1000; increased liver weight, increased macro and microscopic liver pathology, loose feces
Carcinogenicity (2-year dietary)	Rat	NOAEL: 1.8 LOAEL: 18.0; hematotoxicity, chronic nephropathy (M)
Carcinogenicity (18-month dietary)	Mouse	NOAEL: 754.1 LOAEL: Not determined
Two-generation reproduction	Rat	**Parental systemic NOAEL:** 12.7 **Parental systemic LOAEL:** 18.9; decreased body weight, body weight gain, and food consumption, red substance in vagina (F_0), increased mortality (F_1(F)), pale animals, yellow livers (F_1(F)), bile stasis (F_1(F)), and centrilobular necrosis (F_1(F)), decreased absolute, but not relative testes, epididymides, prostate, and brain weights (F_1(M)) **Offspring systemic NOAEL:** 6.3 **Offspring systemic LOAEL:** 12.7; decreased pup body weight (F_1), decreased pup viability at day four (F_1, F_2) **Reproductive NOAEL:** 6.3 **Reproductive LOAEL:** 12.7; Decreased live pups per litter (F_2)

Study Type	Species	Results[a] (mg/kg/day)
Developmental toxicity Dermal	Rat	**Maternal NOAEL:** 300 **Maternal LOAEL:** Not determined **Developmental NOAEL:** 30 **Developmental LOAEL:** 100; increased fetuses and litters with cardiovascular anomalies
Developmental toxicity	Rat	**Maternal NOAEL:** 30 **Maternal LOAEL:** Not determined **Developmental NOAEL:** 3 **Developmental LOAEL:** 10; increased fetuses and litters with cardiovascular anomalies and specifically ventricular septal defect
Developmental toxicity	Rabbit	**Maternal NOAEL:** 1000 **Maternal LOAEL:** 3000; decreased body weight gain and food consumption **Developmental NOAEL:** 3000 **Developmental LOAEL:** Not determined
Developmental toxicity mechanistic	Rat	400; Embryonic death, decreased body weight, and ventricular septal defects all peaked when dams given single oral dose on day 12
Developmental toxicity mechanistic	Rat	400; Embryos exhibited enlarged hearts, edema, and severe anemia when examined days 14-16 of gestation, incidence of interventricular foramen was always greater in treated group than controls
Developmental toxicity mechanistic	Rat & Rabbit	1000; Fetal protoporphyrinogen IX peaks at 12 hours post dosing, rabbits are less susceptible to PPIX accumulation, maternal livers yield less PPIX than embryos in both species
Developmental toxicity mechanistic	Rat & Rabbit	400 and 1000 respectively; Dosing on day 11 provided greatest increase in embryonic PPIX concentrations, rabbits are less susceptible to PPIX accumulation, maternal livers yield less PPIX than embryos in both species
Developmental toxicity mechanistic	Rat	1000; flumioxazin and two related compounds S-23121 and S-23031, compounds that are known to induce developmental effects correlated well with those that increased embryonic PPIX concentrations
Developmental toxicity mechanistic	Rat & Rabbit	1000; Rabbit embryos showed no effects while rat embryos exhibited histopathological hematotoxicity and changes to cardiac tissue without evidence of cell death
Developmental toxicity mechanistic	Rat & Rabbit	Rats excreted radioactive flumioxazin more quickly than rabbits, embryonic concentrations peaked at 4 hours for both species, but the peak was 4 times higher in rats than in rabbits, some unique metabolites were seen in rats
Developmental toxicity mechanistic	Rat & Mouse	Embryonic concentrations peaked at 1 hour for both species, but mice excreted radioactivity more quickly, some unique metabolites were seen in mice
Reverse gene mutation assay	*Salmonella typhimurium/ E.coli*	Negative
In vitro mammalian chromosomal aberration	Chinese hamster ovary cells	Positive at precipitating concentrations with S9 Predominant aberrations were chromatid breaks and exchanges
In vivo mammalian chromosomal aberration	Rat	Negative

Study Type	Species	Results[a] (mg/kg/day)
In vitro unscheduled DNA synthesis	Primary rat hepatocytes	Negative
Hematotoxicity mechanistic	Rat	3000 or 10000 ppm; Sideroblastic regenerative anemia
Hematotoxicity mechanistic	Rat & Mouse	335.8 & 1198.8 respectively; Rats showed hematotoxicity at one and two weeks, but mice did not
Hematotoxicity mechanistic	Dog	1000; Dogs showed no hematotoxicity after two weeks
Hematotoxicity mechanistic	Rat, Mouse, Dog	Relative inhibition of PPO activity by flumioxazin in the liver in vitro was rat > mouse >> dog
Hematotoxicity mechanistic	Rat, Rabbit, Human	Relative inhibition of PPO activity by flumioxazin in the liver in vitro was rat > human > rabbit
Hematotoxicity mechanistic	Rat & Rabbit	Relative inhibition of PPO activity in livers and fetuses in vitro was S-53482 > S-23121 >> S-23031, PPO activity was significantly more inhibited in rat livers and embryos
Metabolism	Rat	**Absorption and excretion** Flumioxazin is absorbed and excreted quickly, mostly within 48 hours. Some saturation of absorption is evident as the urine component of the recovered radioactivity in the high dose is only half that of the low dose. Repeat dosing has little impact on absorption and excretion compared to the single low dose administration. The bile duct cannulation study shows that at the low dose, approximately 90% of the dose is absorbed with approximately half of that returning to the GI tract in bile. Rate and extent of absorption and excretion, non bile duct cannulated (%): Low / High / Repeat Urine 48h: 30.3 ♂, 42.3 ♀ / 12.8 ♂, 22.9 ♀ / 28.1 ♂, 38.8 ♀ Feces 48h: 70.4 ♂, 55.2 ♀ / 84.7 ♂, 76.8 ♀ / 68.4 ♂, 58.4 ♀ Total 48h: 100.7 ♂, 97.5 ♀ / 97.4 ♂, 99.7 ♀ / 96.5 ♂, 97.3 ♀ Rate and extent of absorption and excretion, bile duct cannulated (%): Low Urine 72h: 42.5 ♂, 41.2 ♀ Bile 72h: 42.6 ♂, 39.2 ♀ Feces 72h: 6.1 ♂, 8.7 ♀ GI Tract 72h: 0.8 ♂, 1.7 ♀ Total 72h: 92.0 ♂, 90.8 ♀ T_{max} was found to be 4 hours at low dose then 16 or 8 hours at high dose for males and females respectively. The half life in whole blood was 12 hours at the low dose, but 28 and 46 hours for males and females respectively at the high dose. C_{max} was only 20-fold higher at high dose despite the 100-fold higher dose. **Distribution** Seven days after dosing, the primary sources of radioactivity were blood and blood cells, followed by the liver, kidney and heart at low and repeat dose or thyroid, liver, kidney, lung, spleen, heart at high dose. Bone marrow was not included in the examination.

Study Type	Species	Results[a] (mg/kg/day)
		Metabolism Thirty-five metabolites in total, of which seven, constituting 37.5/46.1% ♂/♀ of total radioactivity, were identified in the low dose and 70.7/71.5% in the high dose. Untransformed parent in low and repeat doses accounted for ~0.3% in males and up to 5.2% in females (though only around 2.2% if a possible outlier is excluded). Parent accounted for 51.0% and 46.6% in high dose males and females. Parent always accounted for less than 0.5% of radioactivity in urine.

[a] Effects observed in both males and females unless otherwise reported

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Flumioxazin

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	CAF/ MOE
Acute dietary, Females aged 13+	NOAEL = 3	Rat developmental toxicity study	Increased incidence of fetal malformations and deaths at non-maternally toxic doses	1000
	ARfD (females 13+) = 0.003 mg/kg bw/day			
Chronic dietary, females aged 13+	NOAEL = 3	Rat developmental toxicity study	Increased incidence of fetal malformations and deaths at non-maternally toxic doses	1000
	ADI (females 13+) = 0.003 mg/kg bw/day			
Chronic dietary, general population	NOAEL = 1.8	Rat chronic toxicity/oncogenicity study	Hematotoxicity and chronic nephropathy	100
	ADI (general population) = 0.02 mg/kg bw/day			
Acute oral	NOAEL = 3	Rat developmental toxicity study	Increased incidence of fetal malformations and deaths at non-maternally toxic doses	1000
All durations dermal	NOAEL = 30	Dermal rat developmental toxicity study	Increased incidence of fetal malformations at non-maternally toxic doses	1000
Short and intermediate inhalation	NOAEL = 3	Rat developmental toxicity study	Increased incidence of fetal malformations and deaths at non-maternally toxic doses	1000

Table 5 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN SOYBEANS		PMRA # 1437715
Radiolabel Position	**[Phenyl- ^{14}C]**	**[THP-^{14}C]**
Test site	Greenhouse	
Treatment	Applied uniformly to soil surface three days after planting	
Rate	99 or 198 g a.i./ha	99 or 198 g a.i./ha
End-use product	Radiolabelled compound dissolved in acetone.	
Preharvest interval	Immature whole plants were harvested 53 days after treatment (DAT) for immature forage and immature forage hay; mature plants (seeds, pods and straw) were harvested at 138 DAT.	

NATURE OF THE RESIDUE IN SOYBEANS	PMRA # 1437715

Total radioative residues (TRRs) were determined in each matrix by combustion and liquid scintillation counting (LSC). In [phenyl-^{14}C]-labeled crops, TRRs were 0.055 ppm and 0.108 ppm in immature forage, 0.155 ppm and 0.348 ppm in immature forage hay, 0.033 ppm and 0.055 ppm in soybean seeds, 0.060 ppm and 0.118 ppm in soybean pods and 0.152 ppm and 0.176 ppm in mature soybean straw, for the low (99 g a.i./ha) and high (198 g a.i./ha) treatment rates, respectively. In [THP-^{14}C]-labeled crops, TRRs were 0.069 ppm and 0.196 ppm in immature forage, 0.257 ppm and 0.617 ppm for immature forage hay, 0.245 ppm and 0.177 ppm for seeds, 0.326 ppm and 0.551 ppm for pods and 0.207 and 0.254 ppm for mature straw, for the low and high treatment rates, respectively.

The majority of the residues (35.9% to 70.8% of the TRRs) in forage, hay and seeds were extractable with acetone/water (4:1, v/v). Extracts were characterized by high performance liquid chromatography (HPLC) and/or thin layer chromatography (TLC) and metabolites were identified by comparison of retention times with those of known standards. Flumioxazin was only detected at low levels (<9.1% TRRs, <0.030 ppm), indicating that it is extensively metabolized in soybean matrices. The only major metabolite identified was 1-OH-HPA in [THP-^{14}C]-labeled matrices.

The predominant metabolic pathway for flumioxazin in soybeans appears to be the cleavage of the imido bond in the parent molecule, followed by hydrolysis and hydroxylation reactions to form the metabolite 1-OH-HPA. A significant proportion of this metabolite appears to be bound to natural plant constituents.

Metabolites Identified	**Major Metabolites (> 10% TRRs)**		**Minor Metabolites (< 10% TRRs)**	
Matrix	**[Phenyl-^{14}C]**	**[THP-^{14}C]**	**[Phenyl-^{14} C]**	**[THP-^{14}C]**
Immature Soybean Forage	None	1-OH-HPA	Flumioxazin APF 482-HA	Flumioxazin THPA
Immature Soybean Forage Hay	None	1-OH-HPA	Flumioxazin APF 482-HA	Flumioxazin THPA
Soybean Seed	None	1-OH-HPA	None	Flumioxazin THPA

NATURE OF THE RESIDUE IN PEANUTS		PMRA # 1437724
Radiolabel Position	**[Phenyl- ^{14}C]**	**[THP-^{14}C]**
Test site	Greenhouse	
Treatment	Incorporated into soil and applied as a 1 cm layer to each plot three days after planting	
Rate	111 or 334 g a.i./ha	111 or 334 g a.i./ha
End-use product	Radiolabelled compound dissolved in acetonitrile.	
Preharvest interval	Mature peanuts (nutmeat, hulls), stems and leaves were harvested 194 days after treatment (DAT) for lower application rate and 245 days after planting (DAP) for higher application rate.	

NATURE OF THE RESIDUE IN PEANUTS		PMRA # 1437724	
TRRs were determined by LSC following combustion. TRRs were 0.009-0.021 ppm in stems and leaves, 0.019-0.020 ppm in hulls, 0.013-0.036 ppm in nutmeat coats and 0.012-0.031 ppm in nutmeats in crops treated at the low rate (111 g a.i./ha). In crops treated at the higher rate (334 g a.i./ha), TRRs were 0.023-0.027 ppm in stems and leaves, 0.097-0.166 ppm in hulls, 0.045-0.085 ppm in nutmeat coats and 0.044-0.093 ppm in nutmeats. Residues were extractable with acetone/water (4:1, v/v). A significant proportion of the residues remained bound (50.5-83.1% of the TRRs). In an attempt to release bound residues, samples from the 1x treatment were treated sequentially with cellulase, 2N HCl and 2N NaOH. Extracts were characterized by HPLC and/or TLC and metabolites were identified by comparison of retention times with those of known standards. Flumioxazin was only detected at low levels (<0.7% TRRs, <0.001 ppm), indicating that it is extensively metabolized in peanut matrices. The chromatographic profile of all matrices indicated four diffuse regions of radioactivity (designated at Regions A-D), likely containing several minor metabolites. The metabolism of flumioxazin peanuts is proposed to occur through the initial opening of the imido ring with subsequent hydrolysis and hydroxylation reactions of the metabolites.			
Metabolites Identified	**Major Metabolites (> 10% TRRs)**		**Minor Metabolites (< 10% TRRs)**	
Radiolabel Position	**[Phenyl-^{14}C]**	**[THP-^{14}C]**	**[Phenyl-^{14}C]**	**[THP-^{14}C]**
Peanut Hulls	None	None	Flumioxazin	Flumioxazin 1-OH-HPA THPA
Peanut Vines	None	None	Flumioxazin	None
Peanut Nutmeats	None	None	None	None

NATURE OF THE RESIDUE IN GRAPES		PMRA # 1437713
Radiolabel Position	**[Phenyl- ^{14}C]**	**[THP-^{14}C]**
Test site	Greenhouse-grown grape vines	
Treatment	A single soil-directed spray application in a prescribed 25 cm diameter surrounding the vines.	
Rate	600 g a.i./ha	
End-use product	Radiolabelled compound dissolved in acetonitrile	
Preharvest interval	Mature grapes and shoots were harvested 91 days after treatment (DAT)	
TRRs were determined in each matrix by combustion and LSC. In [phenyl- ^{14}C]-treated plants, TRRs ranged from 0.0020-0.0021 ppm in grapes (fruit) and from 0.012-0.015 ppm in shoots. In [THP-^{14}C]-treated plants, TRRs ranged from 0.0046-0.0062 ppm in grapes and from 0.039-0.041 ppm in shoots. The majority of the residues (78% to 89%) were extractable with acetone and acetone/water (1:1, v/v) and were characterized as aqueous soluble. Extracted residues in grapes (fruits) were <0.01 ppm and were not characterized further. Extracts in grape shoots were characterized by HPLC. HPLC chromatograms contained multiple peaks, indicating that flumioxazin was extensively metabolized in grape matrices. Metabolites were not identified within the study. Given the low TRRs and limited characterization of residues in grapes, the metabolic profile of flumioxazin in grapes could not be determined.		

NATURE OF THE RESIDUE IN APPLES		PMRA # 1437720
Radiolabel Position	**[Phenyl-^{14}C]**	**[THP-^{14}C]**
Test site	Field-grown apple trees in established orchard	
Treatment	Two soil-directed spray applications at a 60-day retreatment interval; applied uniformly to bare ground and lower portion (30 cm.) of the trunk	
Rate	945 g a.i./ha	934 g a.i./ha
End-use product	Chateau™ WDG (water dispersible granule)	
Preharvest interval	Immature apples (fruit only) were harvested 46 days after the first application; mature apples and foliage were collected 60 days after the last application (DALA).	
TRRs were determined in each matrix by combustion and LSC. TRRs were 0.002 ppm in immature apples. In mature apples, TRRs were 0.001 ppm in [phenyl-^{14}C]-treated fruit and 0.003 ppm in [THP-^{14}C]-treated fruit. Given that TRRs were just above background in all samples, and below the trigger value for further analysis (0.01 ppm), no characterization or identification of metabolites in apples was attempted.		
Overview of the Plant Metabolism Studies		
Flumioxazin was labelled in the phenyl ring or the tetrahydrophthalimide (THP) moiety in all studies. Flumioxazin was applied directly to the soil in all studies. Minimal uptake or translocation into edible matrices was noted with all crops. The predominant metabolic pathway for flumioxazin in plants appears to be the cleavage of the imido bond to produce 482-HA, which is further hydrolyzed to APF and THPA. The hydration of the double bond of the THP ring in THPA yields 1-OH-HPA, which was identified as the major metabolite in soybeans matrices. A significant proportion of the metabolites appear to be bound to natural plant components. The presence of numerous minor peaks in soybeans and diffuse regions of radioactivity in peanuts indicate that flumioxazin is extensively metabolized in plant matrices when applied to the soil. See Figure 1. Based on the metabolism studies in plants, the residue definition for flumioxazin is determined to be the parent, flumioxazin, for purposes of enforcement and risk assessment.		

CONFINED ACCUMULATION IN ROTATIONAL CROPS USING CARROT, LETTUCE AND WHEAT		PMRA # 1442745, 1442746			
Radiolabel Position		**[Phenyl-^{14}C]**		**[THP-^{14}C]**	
Test site		Outdoor plots; planted crops were maintained in screenhouses			
Formulation used for trial		Radiolabeled compound was dissolved in acetone			
Application rate and timing		Flumioxazin was applied to outdoor sandy loam soil plots at rates of 112 or 224 g a.i./ha. Carrot, lettuce and wheat were planted to all plots at 30 days after treatment (DAT) and planted to plots treated at the higher rate (224 g a.i./ha) at 120, 180 and 365 DAT.			
Metabolites Identified		**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Matrix*	**Plantback Interval (days)**	**[Phenyl-^{14}C]**	**[THP-^{14}C]**	**[Phenyl-^{14}C]**	**[THP-^{14}C]**
Wheat, straw	30	Flumioxazin	None	APF 482-HA IMOXA	Flumioxazin 482-HA IMOXA 482-CA
	120	Flumioxazin	Flumioxazin	APF 482-HA IMOXA 482-CA	482-HA 482-CA
	180	None	Flumioxazin	Flumioxazin APF	None

CONFINED ACCUMULATION IN ROTATIONAL CROPS USING CARROT, LETTUCE AND WHEAT				PMRA # 1442745, 1442746	
	365	NA**	Flumioxazin	NA**	None
Wheat, chaff	30	None	None	Flumioxazin APF	Flumioxazin 482-HA
	120	NA**	None	NA**	Flumioxazin 482-HA IMOXA 482-CA
	180	NA**	None	NA**	Flumioxazin 482-HA IMOXA
	365	NA**	None	NA**	Flumioxazin
Carrot, foliage	30	NA**	Flumioxazin	NA**	482-HA IMOXA 482-CA
Carrot, foliage	120	None-	Flumioxazin	None	482-HA IMOXA 482-CA
Carrot, roots	30	NA**	Flumioxazin	NA**	482-HA IMOXA

* Only plant matrices with TRRs * 0.01 ppm were extracted for analysis. For samples with TRRs <0.01 ppm (*i.e.* lettuce, wheat grain), no further analysis or characterization was attempted.
**NA: Not analyzed; due to low TRRs in this matrix, no characterization and/or identification was attempted.

Flumioxazin residues were relatively stable in soil over extended periods of time, eventually degrading to minor components, usually present at levels <0.01 ppm. The low TRRs in rotational crops indicate that flumioxazin and its metabolic degradates are not readily taken up into rotated crops. The only major metabolite identified in rotated crop matrices was the parent, flumioxazin.

NATURE OF THE RESIDUE IN LAYING HEN	PMRA # 1437705, 1437707

Two groups of ten laying hens were administered a single daily oral dose for 14 consecutive days of either [phenyl-^{14}C]-flumioxazin or [THP-^{14}C]-flumioxazin at rates of 9.0-9.9 ppm in feed. The hens were sacrificed *4.5 hours after the final dose was administered.

The majority of the administered dose (AD) was excreted (78.3% to 92.6% AD, including cage wash), and an additional 1.5% to 5.8% AD was recovered in the gastrointestinal tract and gizzard. Eggs and edible tissues contained 0.59% to 0.90% AD. The highest concentration of radioactivity were detected in liver (0.237-1.137 ppm) and kidney (0.272-0.887 ppm). The TRRs in egg whites reached a peak between days 4 and 7 (0.041-0.18 ppm) and TRRs in egg yolks reached a peak between days 11 and 12 (0.437-0.640 ppm).

Residues in tissues and eggs were extracted with organic solvents and extracts were characterized by HPLC and TLC. Metabolites were identified by co-chromatography with available reference standards and/or mass spectrometry (MS).

The metabolism of flumioxazin in poultry appears to proceed via the hydroxylation of the parent compound with the subsequent incorporation of a sulfonic acid group, and the cleavage if the imide linkage within the parent molecule.

Matrices		% of the Administered Dose
	[^{14}C-phenyl]	[^{14}C-THP]
Excreta	93.1	78.3

NATURE OF THE RESIDUE IN LAYING HEN			PMRA # 1437705, 1437707	
Muscle	0.03-0.04		0.05-0.06	
Fat	0.02		0.01	
Liver	0.08		0.27	
Egg	0.36		0.42	
Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**[^{14}C-phenyl]**	**[^{14}C-THP]**	**[^{14}C-phenyl]**	**[^{14}C-THP]**
Liver	None	4-OH-flumioxazin THPA	Flumioxazin APF 482-HA 3-OH-flumioxazin 4-OH-flumioxazin	Flumioxazin 3-OH-flumioxazin 4-OH-THPA 3-OH-flumioxazin-SA 4-OH-flumioxazin-SA OH-flumioxazin
Kidney	None	THPA 4-OH-THPA	Flumioxazin APF 482-HA 3-OH-flumioxazin 4-OH-flumioxazin 3-OH-flumioxazin-SA 4-OH-flumioxazin-SA	Flumioxazin 3-OH-flumioxazin 4-OH-flumioxazin 3-OH-flumioxazin-SA 4-OH-flumioxazin-SA OH-flumioxazin
Thigh Muscle	None	Flumioxazin 4-OH-flumioxazin THPA 4-OH-THPA	Flumioxazin APF 482-HA 3-OH-flumioxazin 4-OH-flumioxazin 3-OH-flumioxazin-SA 4-OH-flumioxazin-SA	3-OH-flumioxazin OH-flumioxazin
Breast Muscle	Flumioxazin APF	Flumioxazin 3-OH-flumioxazin 4-OH-flumioxazin THPA	482-HA 3-OH-flumioxazin 4-OH-flumioxazin 3-OH-flumioxazin-SA 4-OH-flumioxazin-SA	3-OH-flumioxazin 4-OH-flumioxazin 4-OH-THPA OH-flumioxazin
Fat	Flumioxazin	Flumioxazin 3-OH-flumioxazin 4-OH-flumioxazin	3-OH-flumioxazin 4-OH-flumioxazin 3-OH-flumioxazin-SA	THPA 4-OH-THPA OH-flumioxazin
Skin with Fat	Flumioxazin	Flumioxazin 4-OH-flumioxazin THPA	APF 482-HA 3-OH-flumioxazin 4-OH-flumioxazin 3-OH-flumioxazin-SA	3-OH-flumioxazin 4-OH-THPA OH-flumioxazin
Egg Whites	APF 482-HA	THPA TPA 3-OH-THPA 4-OH-THPA	None	Flumioxazin OH-flumioxazin

NATURE OF THE RESIDUE IN LAYING HEN			PMRA # 1437705, 1437707	
Egg Yolks	None	THPA 4-OH-flumioxazin-SA	Flumioxazin APF 482-HA 3-OH-flumioxazin 4-OH-flumioxazin 3-OH-flumioxazin-SA 4-OH-flumioxazin-SA	Flumioxazin 3-OH-flumioxazin 4-OH-flumioxazin 4-OH-THPA 3-OH-flumioxazin-SA OH-flumioxazin

NATURE OF THE RESIDUE IN LACTATING GOAT	PMRA # 1437709, 1437711

Two groups of two lactating goats were administered a single daily oral dose for 5 consecutive days of either [phenyl-^{14}C]-flumioxazin or [THP-^{14}C]-flumioxazin at average doses of 11.8 ppm or 7.2 ppm, respectively, in feed. Goats were sacrificed within 6 hours of the final dose.

The majority of the AD was excreted (65% to 78.8% AD, including cage wash), and an additional 15% to 19% AD was recovered in the gastrointestinal tract. Milk and edible tissues contained 0.42% to 0.78% AD. The highest concentration of radioactivity was detected in liver (0.165-0.330 ppm) and kidney (0.110-0.238 ppm). The TRRs in milk reached a plateau within 1-2 days of initial dosing, with peak concentrations of 0.032-0.055 ppm.

Residues in milk and tissues were extracted with organic solvents and extracts were characterized by HPLC and TLC. Metabolites were identified by co-chromatography with reference standards or isolated metabolites, and/or by MS.

The metabolism of flumioxazin in ruminants appears to proceed via 1) the hydroxylation of the parent molecule with the subsequent incorporation of a sulfonic group, 2) the reduction of the parent molecule and subsequent hydroxylation of the metabolites, and 3) cleavage of the imide and amide linkages of the parent molecule.

Matrices	**% of Administered Dose**			
	[^{14}C-phenyl]		**[^{14}C-THP]**	
Urine and feces	64.9-65.8		73.2-78.8	
Muscle	0.02		0.04-0.05	
Fat	<0.02		0.02	
Kidney	0.01-0.02		0.04-0.05	
Liver	0.12-0.19		0.40-0.44	
Milk	0.05-0.17		0.20-0.22	
Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**[^{14}C-phenyl]**	**[^{14}C-THP]**	**[^{14}C-phenyl]**	**[^{14}C-THP]**
Liver	None	Metabolite F	Flumioxazin 3-OH-flumioxazin-SA 4-OH-flumioxazin-SA 482-HA APF 4-OH-flumioxazin 3-OH-flumioxazin	Flumioxazin 3-OH-flumioxazin 4-OH-flumioxazin 4-OH-THPA SAT-482 THPA Metabolite B
Kidney	4-OH flumioxazin	Metabolite B	Flumioxazin 482-HA APF 3-OH-flumioxazin	3-OH-flumioxazin 4-OH-flumioxazin 4-OH-THPA SAT-482 THPA Metabolite C

NATURE OF THE RESIDUE IN LACTATING GOAT			PMRA # 1437709, 1437711	
Muscle	None	4-OH-flumioxazin Metabolite C	Flumioxazin 482-HA APF 4-OH-flumioxazin 3-OH-flumioxazin	Flumioxazin 4-OH-THPA
Milk	482-HA	Metabolite B Metabolite C	3-OH-flumioxazin-SA 4-OH-flumioxazin-SA APF 4-OH-flumioxazin 3-OH-flumioxazin	4-OH-flumioxazin 4-OH-THPA

Overview of Animal Metabolism Studies

Flumioxazin was radiolabelled in the phenyl ring or the THP moiety for all studies. In livestock, flumioxazin is metabolized either via 1) the hydroxylation of the cyclohexene ring of the THP moiety to yield 3-OH- and 4-OH-flumioxazin, followed by the subsequent incorporation of a sulfonic acid group to the hydroxylated THP moiety to yield 3-OH- and 4-OH-flumioxazin-SA, 2) the reduction at the 1,2-double bond of the THP moiety to yield SAT-482, which can be subsequently hydroxylated at the 3-OH or 4-OH position, or 3) the cleavage of the imide linkage to yield the metabolites 482-HA, APF and THPA. See Figure 1.

Based on the metabolism studies in lactating goat and laying hen, the residue definition for enforcement purposes in ruminants was determined to be flumioxazin and the metabolites 3-OH-flumioxazin and 4-OH-flumioxazin, while the residue definition for enforcement purposes in poultry was determined to be flumioxazin.

The residue definitions for risk assessment were determined to be the following: in ruminant muscle and fat, flumioxazin and the metabolites 4-OH-flumioxazin and Metabolite C; in ruminant meat byproducts, flumioxazin and the metabolites 482-HA, SAT-482, 3-OH-flumioxazin, 4-OH-flumioxazin and Metabolites B, C and F; in milk, flumioxazin and the metabolites 482-HA and Metabolites B and C; in poultry commodities, flumioxazin and the metabolites APF, 3-OH-flumioxazin, 4-OH-flumioxazin, 4-OH-flumioxazin-SA, THPA, 4-OH-THPA and OH-flumioxazin.

Figure 1 Summary of the Metabolic Pathways of Flumioxazin in Animals (Lactating Goats and Laying Hens) and Treated Plants (Soybeans, Peanuts)

STORAGE STABILITY	PMRA # 1288589, 1442698, 1442704, 1442715, 1288648, 1288605

Grape (fruit), soybean forage, hay and seed, cherry fruit, potato tuber: The data indicate that residues of flumioxazin are stable at -20°C for *ca.* 7 months in grapes, *ca.* 9 months in potatoes and *ca.* 12 months in soybean forage, hay and seed and cherry fruit.
Grape raisins, grape juice, dried prunes, wet apple pomace, apple juice: The data from processed commodities indicate that residues of flumioxazin are stable at -20°C for *ca.* 2 months in grape juice, 6 months in raisins, and *ca.* 9 months in dried prunes, wet apple pomace and apple juice.

CROP FIELD TRIALS ON POTATO	PMRA# 1288589

Fourteen (14) residue trials were conducted on potatoes in the United States during the 2001 growing season. The potato trials were conducted in NAFTA Zones 1 (2 trials), 2 (1 trial), 3 (1 trial), 5 (3 trials), 9 (2 trials), 10 (1 trial) and 11 (4 trials). Flumioxazin (formulated as a water dispersible granule (WDG)) was applied in a single pre-emergent application to the soil after the last hilling operation at rates of 123 to 148 g a.i./ha. Mature potato tubers were harvested 62 to 126 days after treatment (DAT).

Commodity	Total Rate (g a.i./ha)	PHI (days)	Flumioxazin Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Potato, tuber	123-148	62-126	28	<0.02	<0.02	<0.02	<0.02	<0.02	0

CROP FIELD TRIALS ON DRY BULB ONION	PMRA# 1452111

Nine (9) residue trials were conducted on dry bulb onions in the United States during the 2001 growing season. The dry bulb onion trials were conducted in NAFTA Zones 1 (1 trial), 2 (1 trial), 5 (1 trial), 5A (1 trial), 6 (1 trial), 9 (1 trial), 10 (2 trials) and 11 (1 trial). Flumioxazin (WDG) was applied twice as a post-emergent broadcast spray at a rate of 101-116 g a.i./ha for a total application rate of 208-224 g a.i./ha (*300% of the maximum Canadian recommended seasonal rate of 71 g a.i./ha). A non-ionic surfactant (NIS) was included with each application at a rate of 0.25% v/v. The applications were made at 29-78 day intervals and mature onions were harvested at preharvest intervals (PHIs) of 42-49 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Flumioxazin Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Onion, bulb	208-224	42-49	18	<0.02	<0.02	<0.02	<0.02	<0.02	0

CROP FIELD TRIALS ON SOYBEANS	PMRA# 1442703, 1442705, 1442724

Forty-three (43) residue trials were conducted on soybeans in Canada and the United States during the 1989, 1990, 1992 and 1993 growing seasons. The soybean trials were conducted in NAFTA Zones 2 (2 trials), 4 (10 trials), 5 (30 trials) and 5B (1 trial). Flumioxazin (formulated as either a WDG, a wettable powder (WP) or a flowable (FL)) was applied as a single pre-emergent soil application (either pre-plant incorporated (PPI), shallow pre-plant incorporated (SHIN), pre-emergent (PRE) or pre-emergent, no-till (NT)) at a rate of 101-109 g a.i./ha. A petroleum based crop oil concentrate was included with most WDG and WP applications, at a rate of 1% v/v. Soybean forage samples were harvested at PHIs of 21-67 days, soybean hay was harvested at PHIs of 49-179 days and allowed to field dry for 1-13 days and mature seeds were harvested at PHIs of 111-166 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Flumioxazin Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Soybean, Forage	101-109	21-67	151	<0.02	0.03	0.03	<0.02	<0.02	0
Soybean, Hay	101-109	49-179	84	<0.02	<0.02	<0.02	<0.02	<0.02	0
Soybean Seed	101-109	111-166	86	<0.02	<0.02	<0.02	<0.02	<0.02	0

RESIDUE DECLINE IN SOYBEANS	PMRA# 1442705

At two sites, treated samples of whole immature soybean plants were collected at 7-8, 15, 29-30, 39-40, 60 and 90 DAT. Quantifiable residues up to 0.07 ppm were noted in one trial up to 15-DAT, but residues subsequently declined to <LOQ (<0.02 ppm) by 30-DAT. No quantifiable residues were found at any PHI in the second decline trial.

CROP FIELD TRIALS ON POME FRUITS							PMRA# 1288605, 1442700		
Eighteen (18) residue trials were conducted on pome fruits in the United States during the 2002 and 2003 growing seasons. The apple trials were conducted in NAFTA Zones 1 (3 trials), 2 (1 trial), 5A (2 trials), 9 (1 trial), 10 (1 trial) and 11 (4 trials) for a total of 12 trials. The pear trials were conducted in NAFTA Zones 1 (1 trial), 10 (2 trials), and 11 (3 trials) for a total of six trials. Flumioxazin (FL or WDG) was applied twice as a soil-directed application at a rate of 419-445 g a.i./ha/ application for a seasonal application rate of 845-886 g a.i./ha (*800% maximum Canadian recommended seasonal rate of 107 g a.i./ha). The applications were made at 53-64 day intervals and mature fruit were harvested at PHIs of 56-61 days.									
Commodity	**Total Rate (g a.i./ha)**	**PHI (days)**	**Flumioxazin Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
Apple, fruit	845-886	56-60	24	<0.02	<0.02	<0.02	<0.02	<0.02	0
Pear, fruit	853-873	59-61	12	<0.02	<0.02	<0.02	<0.02	<0.02	0
RESIDUE DECLINE IN APPLES							**PMRA# 1228605**		
At one site, treated samples were collected at PHIs of 45, 52, 60, 68 and 72 days. No quantifiable residues of flumioxazin were detected in the earliest sample (45-day PHI), therefore residue decline could not be assessed.									

CROP FIELD TRIALS ON STONE FRUITS							PMRA# 1442698, 1442699, 1442704		
Twenty-one (21) residue trials were conducted on stone fruits in the United States during the 2002 and 2003 growing seasons. The cherry trials were conducted in NAFTA Zones 1 (1 trial), 5A (2 trials), 10 (1 trial) and 11 (2 trials) for a total of 6 trials. The peach trials were conducted in NAFTA Zones 1 (1 trial), 2 (3 trials), 5A (1 trial), 6 (1 trial) and 10 (3 trials) for a total of 9 trials. The plum trials were conducted in NAFTA Zones 5A (1 trial), 10 (4 trials) and 11 (1 trial) for a total of 6 trials. Flumioxazin (FL or WDG) was applied twice as a soil-directed application at a rate of 413-445 g a.i./ha/application for a seasonal application rate of 843-882 g a.i./ha (*800% maximum Canadian recommended seasonal rate of 107 g a.i./ha). The applications were made at 15-64 day intervals and mature fruit were harvested at PHIs of 53-61 days.									
Commodity	**Total Rate (g a.i./ha)**	**PHI (days)**	**Flumioxazin Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
Cherry, fruit	845-860	59-61	12	<0.02	<0.02	<0.02	<0.02	<0.02	0
Peach, fruit	854-882	53-60	18	<0.02	<0.02	<0.02	<0.02	<0.02	0
Plum, fruit	843-875	60-61	12	<0.02	<0.02	<0.02	<0.02	<0.02	0
RESIDUE DECLINE IN PLUM							**PMRA# 1442704**		
At one site, treated samples were collected at PHIs of 46, 53, 60, 68 and 75 days. No quantifiable residues of flumioxazin were detected in the earliest sample (46-day PHI), therefore residue decline could not be assessed.									

CROP FIELD TRIALS ON BLUEBERRY	PMRA# 1500898

Six (6) residue trials were conducted on blueberries in the United States during the 2003 growing season. The blueberry trials were conducted in NAFTA Zones 1 (1 trial), 2 (2 trials), 5A (2 trials), and 12 (1 trial). At five sites, flumioxazin (WDG) was applied to highbush blueberries twice as soil-directed applications at a rate of 415-452 g a.i./ha/application for a total application rate of 834-891 g a.i./ha (*800% of the maximum Canadian recommended seasonal rate of 107 g a.i./ha). Applications were made at 50-113 day intervals and mature blueberries were harvested at PHIs of 6-8 days. At the remaining site, flumioxazin (WDG) was applied to lowbush blueberries as a single broadcast application to dormant plants at a rate of 448 g a.i./ha, and mature blueberries were harvested 99 DAT.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Flumioxazin Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Blueberry, lowbush	448	99	2	<0.02	<0.02	<0.02	<0.02	<0.02	--
Blueberry, highbush	837-942	6-8	10	<0.02	<0.02	<0.02	<0.02	<0.02	0

CROP FIELD TRIALS ON GRAPE	PMRA# 1288648

Twelve (12) residue trials were conducted on grapes in the United States during the 1999 growing season. The grape trials were conducted in NAFTA Zones 1 (2 trials), 10 (9 trials) and 11 (1 trial). Flumioxazin (WDG) was applied twice as soil-directed applications to row middles and berms at a rate of 398-434 g a.i./ha/application for a total seasonal application rate of 824-858 g a.i./ha (*800% of the maximum Canadian recommended seasonal rate of 107 g a.i./ha). At three sites, grapes were treated at an exaggerated rate of 826-860 g a.i./ha/application for a total application rate of 1656-1703 g a.i./ha. A crop oil concentrate was applied at most sites at a rate of 2.3 L/ha. Applications were made at 58-62 day intervals and mature grapes were harvested at PHIs of 69-60 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Grape, fruit	824-858	59-60	24	<0.01	<0.01	<0.01	<0.01	<0.01	0
	656-1703	60	6	<0.01	<0.01	<0.01	<0.01	<0.01	0

CROP FIELD TRIALS ON STRAWBERRY	PMRA# 1281542

Eight (8) residue trials were conducted on strawberries in the United States during the 2002 growing season. The strawberry trials were conducted in NAFTA Zones 1 (1 trial), 2 (1 trial), 3 (1 trial), 5A (1 trial), 10 (3 trials) and 12 (1 trial). At three sites, flumioxazin (WDG) was applied twice to perennial-type strawberries, as a single soil-directed application at dormancy, followed by a post-directed (shielded) application to row middles at rates of 104-110 g a.i./ha/application for total application rates of 210-220 g a.i./ha. Applications were made at 69-120 day intervals. At the remaining five sites, flumioxazin (WDG) was applied to annual-type strawberries as a single post-directed (shielded) application to the row middles at a rate of 105-108 g a.i./ha. Mature strawberries were harvested at PHIs of 1-2 days from all trial sites.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Strawberry, fruit	105-108	1-2	10	<0.02	0.05	0.043	0.02	0.03	0.01
	210-220	1	6	<0.02	0.034	0.028	0.02	0.02	0.006

CROP FIELD TRIALS ON ASPARAGUS	PMRA# 1500897

Eight (8) residue trials were conducted on asparagus in the United States during the 2003 and 2004 growing seasons. The asparagus trials were conducted in NAFTA Zones 2 (1 trial), 5A (2 trials), 10 (3 trials) and 11 (2 trials). Flumioxazin (WDG) was applied in a single broadcast application to dormant plants at rates of 213-221 g a.i./ha or 427-452 g a.i./ha. Mature asparagus spears were harvested at PHIs of 8-20 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Asparagus, spears	213-221	8-20	16	<0.02	<0.02	<0.02	<0.02	<0.02	0
	427-452	8-20	16	<0.02	<0.02	<0.02	<0.02	<0.02	0

PROCESSED FOOD AND FEED	PMRA # 1442705, 1442724, 1288589, 1442704, 1288605, 1288648

Processing studies were conducted on potatoes, soybeans, apples, plums and grapes. As residues of flumioxazin were <LOQ (<0.02 ppm) in all raw agricultural commodities (RACs; *i.e.* potato tuber, soybean seed, apple fruit, plum fruit and grape fruit) and all processed commodities, it was not possible to determine if residues concentrated into these matrices.

LIVESTOCK FEEDING - DAIRY COW	PMRA # 1442755

In the feeding study, flumioxazin was administered orally in gelatin capsules to three groups of lactating cows (three cows/group) once daily for 28 consecutive days. Based on average feed consumption, the treatment rates corresponded to 2 mg/kg, 6 mg/kg and 20 mg/kg feed.

Milk and tissues (liver, muscle, fat and kidney) were analyzed for flumioxazin and the metabolites 3-OH-flumioxazin and 4-OH-flumioxazin. No quantifiable residues of any metabolite were detected in milk, liver, kidney, muscle and fat samples from cows fed flumioxazin at a rate of 20 mg/kg in their diet.

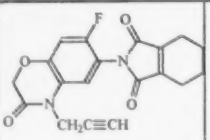
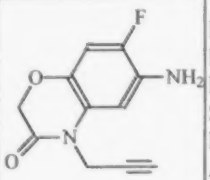
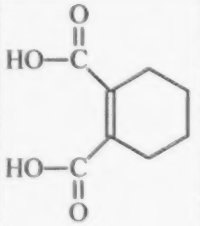
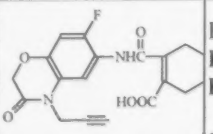
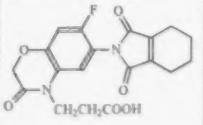
Table 6 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

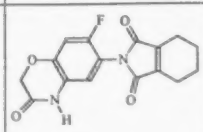
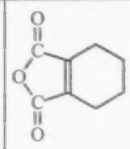
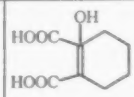
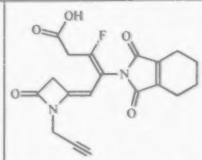
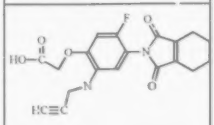
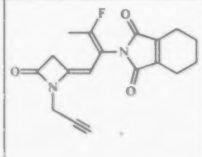
PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops (soybean, peanut, grape, apple)** **Rotational crops**	Flumioxazin Flumioxazin
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops** **Rotational crops**	Flumioxazin Flumioxazin
METABOLIC PROFILE IN DIVERSE CROPS	The metabolic profile is similar between soybeans, peanuts, grapes and apples

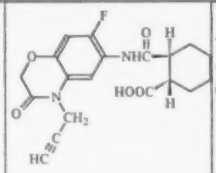
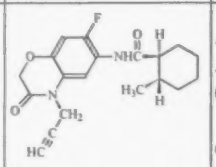
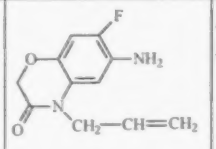
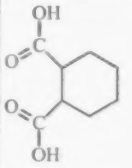
ANIMAL STUDIES	
ANIMALS	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT	Flumioxazin and the metabolites 3-OH-Flumioxazin and 4-OH-Flumioxazin
RESIDUE DEFINITION FOR RISK ASSESSMENT	In muscle & fat: Flumioxazin and the metabolites 4-OH-Flumioxazin and Metabolite C In meat byproducts: Flumioxazin and the metabolites 482-HA, SAT-482, 3-OH-Flumioxazin, 4-OH-Flumioxazin and Metabolites B, C and F In Milk: Flumioxazin and the metabolites 482-HA and Metabolites B and C
ANIMALS	**Poultry**
RESIDUE DEFINITION FOR ENFORCEMENT	Flumioxazin
RESIDUE DEFINITION FOR RISK ASSESSMENT	Flumioxazin and the metabolites APF, 3-OH-Flumioxazin, 4-OH-Flumioxazin, 4-OH-Flumioxazin-SA, THPA, 4-OH-THPA and OH-Flumioxazin
METABOLIC PROFILE IN ANIMALS (goat, hen, rat)	The metabolic profile is similar between goat, hen and rat
FAT SOLUBLE RESIDUE	Yes

ANIMAL STUDIES			
DIETARY RISK FROM FOOD AND WATER			
Basic chronic non-cancer dietary risk **ADI (general population) = 0.02 mg/kg bw/day** **ADI (females, 13-49 yrs old) = 0.003 mg/kg bw/day** **Estimated chronic drinking water concentration = 47 µg a.i./L (Level 1)**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
	All infants < 1 year	1.9	2
	Children 1–2 years	3.6	3.7
	Children 3 to 5 years	3	3.1
	Children 6– 12 years	1.8	1.9
	Youth 13–19 years	1	1
	Adults 20–49 years	0.7	0.8
	Adults 50+ years	0.7	0.8
	General population	1.1	1.1
	Females 13-49 years	5	5.5
Basic acute dietary exposure analysis, 95th percentile **Estimated acute drinking water concentration = 51 µg a.i. /L (Level 1)**	**POPULATION**	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Only	**Food and Water**
ArfD (females 13-49 years) = 0.003 mg/kg bw/day	**Females 13–49 years**	12.7	14.2

Table 7 Major and Minor Transformation Products

Transformation Product (CAS No.)	Structure	Transformation Process	% Max (day)	% at Study termination	Mobility
Flumioxazin (Parent) 2-[7-fluoro-3,4-dihydro-3-oxo-4-(2-propynyl)-2*H*-isoindole-1,3(2H)-dione					Kd: 0.47-24.0 Koc: 11.5-1708 low mobility to very high mobility
APF 6-amino-7-fluoro-4-(2-propynyl)-2*H*-1,4-benzoxoazin-3(4*H*)-one		**Hydrolysis pH 5** **Hydrolysis pH 7** Hydrolysis pH 9 Soil Phototransformation **Anaerobic soil biotransformation** **Anearobic sediment biotransformation**	86.6 80.0 Minor Minor 59.2 59.0	86.6[2] 80.0[2] 4.13 ND	Kd: 1.6-6.0 Koc:201-620 low to medium mobility
THPA 3,4,5,6-tetrahydrophthalic acid		**Soil** **Phototransformation** **Water photolysis** **Hydrolysis pH 5** **Hydrolysis pH 7** Hydrolysis pH 9 Aerobic Soil **Anearobic Aquatic** Anearobic sediment	 12.9 18.0 99.9 (21) 83.6 ND 6.6 41.9 (0) 49.5 (1)	 12.9[2] 18.0 96.6[2] 83.6[2] ND ND 0.79 ND (59)	Kd:0.11-5.3 Koc:13-339 medium to very high mobility
482-HA N-[7-fluoro-3-oxo-4-(2-propynyl)-2H-1,4-benzoxazin-6-yl]-3,4,5,6-tetrahydrophthalamic acid		Hydrolysis pH 5 **Hydrolysis pH 7** **Hydrolysis pH 9** Soil Phototransformation (minor) **Aerobic/Anearobic biotransformation study** **Anearobic water/soil**:	6.7(8hrs.) 70.3 (2) 102.2 (4) 1.4 (0) 7.23 52.8 (1)	Minor 8.3 96.1[2] 0.6 7.23[2] N.D.	Based on structure expected to be very highly mobile
482-CA 2-[7-fluoro-3-oxo-6-(3,4,5,6-tetrahydrophthalimido)-2H-1,4-benzoxazin-4-yl]		Aerobic soil	0.7 (30)	0.1	-

Transformation Product (CAS No.)	Structure	Transformation Process	% Max (day)	% at Study termination	Mobility
propionic acid					
IMOXA 2-[7-fluoro-3,4-dihydro-3-oxo-2*H*-1,4-benzoxazin-6-yl]-4,5,6,7-tetrahydro-1H-isoindole-1,3(2H)-dione		Soil Phototransformation Aerobic Soil	3.1 3.0 (63)	3.1 2.0	-
Δ ³-TPA 3,4,5,6-Tetrahydrophthalic acid anhydride		**Soil** **Phototransformation** Hydrolysis pH5 Hydrolysis pH 7 Hydrolysis pH Aerobic Soil	21.6 (9) 5.1 (21) 6.15 (14) ND 5.1 (5)	8.6 Minor Minor ND Minor	-
1-OH-HPA 1-hydroxy-*trans*-1,2-cyclohexanedicarboxylic acid		**Soil** **phototransformation** Anearobic Aquatic	4.4 4.8 (21)	4.4[2] ND (42)	-
482-PHO	 (structure proposed by applicant - not probable)	**Water photolysis**	69.0 (4 hrs)		-
	 (probable alternate structure)				
482-PHO-ISO	unknown	**Water photolysis**	15 (24 hrs)		-
482-PHO-DC		**Water photolysis**	10 (48 hrs)		-

Transformation Product (CAS No.)	Structure	Transformation Process	% Max (day)	% at Study termination	Mobility
SAT-482-HA[1] *N*-[7-fluoro-3-oxo-4-(2-propynyl)-2*H*-1,4-benzoxazin-6-yl]-2-*cis*-carbamoylcyclo-hexanecarboxylic acid		Anearobic Aquatic **Anearobic Aquatic (sediment)**	8.7 (268) 10.7	6.8 10.6[2]	-
SAT-482-HA-2[1] *N*-[7-fluoro-3-oxo-4-(2-propynyl)-2*H*-1,4-benzoxazin-6-yl]-2-*trans*-carbamoylcyclo-hexanecarboxylic acid		**Anearobic soil** Anaerobic Aquatic (total system-16.9% day 182, declined to 11% at day 360)	16.2 16.9(182)	16.2[2] 11 (360)	-
DAPF[1]		**Anaerobic Aquatic/sediment**	20.7	20.7[2]	-
HPA[1] *trans*-1,2-cyclohexandedicarboxylic acid		**Anearobic Aquatic/sediment**	86.3	86.3[2]	-
Adipic Acid		**Water photolysis**	11	11[2]	-
Others (max peak of single compound no greater than 9%)	unknown	**Water photolysis** **Anearobic aquatic/sediment**	70 7.8	70[2] 7.8[2,3]	-
Unknown 1	unknown	**Water photolysis**	11	11[2]	-
Area 3	unknown	Soil phototransformation	1.6	1.6	-
UP-3	unknown	Anearobic aquatic	5.5 (42)	2.3	-

Transformation Product (CAS No.)	Structure	Transformation Process	% Max (day)	% at Study termination	Mobility
UP-1	unknown	Anearobic aquatic	13.6 (59)	4.7	-
TU-1	unknown	Anearobic aquatic	5.5 (10)	0.34	-

Shaded area indicates that the transformation product was included in the drinking water assessment.
Bold text indicates 'major transformation product"
[1] Transformation Product was only included in the Surface Water Drinking Water Assessment. It was not included in the groundwater assessment.
[2] Transformation product increasing at study termination.
[3] This value is comprised of many small compounds
- Indicates that no data was provided.

Table 8 Fate and Behaviour of Flumioxazin in the Terrestrial Environment

Property	Value		Major transformation products	Bound Residues	Classification	References
Abiotic transformation						
Hydrolysis ($t_{1/2}$) pH 5 pH 7 pH 9	PH-label 6.3 days 19.2 hours 26 minutes	THP-label 3.4 days 16.8 hours 14.4 minutes	**APF, THPA** 482-HA, **APF, THPA** **482-HA**	N/A	Expected to be an important route of transformation	1437738 1437740
Hydrolysis: 482-HA ($t_{1/2}$) pH 5 pH 7 pH 9	Not a major transformation product at pH 5 5.4 days stable		N/A	N/A	N/A	1437738 1437740
Phototransformation on soil ($t_{1/2}$) (12 h light: 12 h dark cycle)	PH label 4.5 days	THP label 8.4 days	Δ-TPA, **THPA** Minor accumulating transformation products: **IMOXA, 1-OH-HPA**	PH label: 17.1-43.3% THP label:5.0-9.3%	Not expected to be an important route of transformation	1437742 1437744
Phototransformation in air	No data is required as flumioxazin is not expected to be volatile under field conditions.					
Biotransformation						
Biotransformation in aerobic soil (DT_{50})	5.0-111 days		CO_2, **bound residues**	PH label: ≤ 74% THP: ≤ 29.0%	Non-persistent to moderately persistent	1437749 1437751 1437753 1445305

Property	Value	Major transformation products	Bound Residues	Classification	References
Biotransformation in anaerobic soil (DT_{50})	9.0-9.8 hours	482-HA (water), **SAT-482-HA-2** (water), **uncharacterized polar products** (water and soil), **bound residues**, CO_2	PH label: ≤ 60% THP: ≤ 23%	Non-persistent	1437755 1445305
Mobility					
Adsorption / desorption in soil (Koc) APF sandy loam Loam Sandy loam Sandy loam Sediment THPA sandy loam Loam Sandy loam Sandy loam Clay Sediment	 336 391 502 620 201 13 248 66 339 191 75	N/A		 Medium mobility Medium mobility Low mobility Low mobility Medium mobility Very high mobility Medium mobility	1437759 1437761
Column leaching flumioxazin (Koc) PH label Sand Sandy loam Silt loam Clay loam	 26 11.5 1708 81	N/A	N/A	 Very high mobility Very high mobility Low mobility High mobility	1437763
Column Leaching Flumioxazin (Koc) THP label Sand Sandy loam Silt loam Clay loam	 227 105 675 497	N/A	N/A	 Medium mobility High mobility Low mobility Medium mobility	1437765
Volatilization	Not required as flumioxazin is not expected to be volatile under field conditions.				

Property	Value	Major transformation products	Bound Residues	Classification	References
Field studies					
Field dissipation	DT_{50}: 4-38 days	N/A	N/A	Non-persistent to Moderately persistent	1430428 1430423 1442767 1442777
Bold text indicates that the transformation products were stable or continuing to increase in concentration at study termination.					

Table 9 Fate and Behaviour of Flumioxazin in the Aquatic Environment

Property	Value		Major transformation products	Bound Residues	Classification	References
Abiotic transformation						
Hydrolysis pH 5 pH 7 pH 9	PH-label 6.3 days 19.2 hours 26 minutes	THP-label 3.4 days 16.8 hours 14.4 minutes	**APF, THPA** 482-HA, **APF, THPA** **482-HA**	N/A	Expected to be an important route of transformation	1437738 1437740
Hydrolysis: 482-HA pH 5 pH 7 pH 9	Not a major transformation product at pH 5 5.4 days stable		N/A	N/A	N/A	1437738 1437740
Phototransformation in water (12 h light: 12 h dark cycle)	PH label 1.02 hours	THP label 1.01 hours	482-PHO, 482-PHO-ISO, 482-PHO-DC, **THPA, Adipic Acid, Unknown 1, Other, CO_2**	N/A	Important route of transformation in the photic zone of aquatic systems.	1609727 1437746
Phototransformation in air	No data is required as flumioxazin is not expected to be volatile under field conditions.					
Biotransformation						
Biotransformation in aerobic water systems	An aerobic water/sediment study is required as per the PMRA Regulatory Directive DIR2003-03. Since a study has not been submitted, the fate of flumioxazin and its transformation products have not been characterized in aerobic aquatic environments.					
Biotransformation in anaerobic water systems	$t_{1/2}$: 1.1-1.42 days $t_{9/10}$: 27.9-34.3 days		APF, **DAPF, SAT-482-HA** (PH label only), THPA, **HPA, UP-1, bound residues** (PH label only)	PH label: 30% THP label:4%	Non-persistent	1437756
Mobility						
Adsorption / desorption in soil			N/A			1437759 1437761

Property	Value	Major transformation products	Bound Residues	Classification	References
(Koc) APF sandy loam Loam Sandy loam Sandy loam Sediment THPA sandy loam Loam Sandy loam Sandy loam Clay Sediment	 336 391 502 620 201 13 248 66 339 191 75 N/A			 Medium mobility Medium mobility Low mobility Low mobility Medium mobility Very high mobility Medium mobility High mobility Medium mobility Medium mobility Low mobility	
Column leaching flumioxazin (Koc) PH label Sand Sandy loam Silt loam Clay loam	 26 11.5 1708 81	N/A	N/A	 Very high mobility Very high mobility Low mobility High mobility	1437763
Column Leaching Flumioxazin (Koc) THP label Sand Sandy loam Silt loam Clay loam	 227 105 675 497	N/A	N/A	 Medium mobility High mobility Low mobility Medium mobility	1437765
Bold text indicates that the transformation products were stable or continuing to increase in concentration at study termination.					

Table 10 Effects on Terrestrial Organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Reference
Invertebrates					
Earthworm	Acute	Flumioxazin	LC_{50} >982 mg a.i./kg soil NOEC 61 mg a.i./kg soil	N/A	1437776
Bee	Oral	Unknown*	LD_{50} >100 µg a.i./bee LD_{50} >200 µg 50% WP/bee*	Relatively non-toxic	1437574
	Contact	Flumioxazin	LD_{50} >105 ug ai/bee NOEC 105 ug a.i./bee	Relatively non-toxic	1437778
	Brood / hive	Study not provided and is not required since flumioxazin was relatively non-toxic on a contact basis and the mode of action is not expected to affect the growth of juvenile honeybees.			
Predatory arthropod *T. pyri* *P. cupreus* *C. carnea* *A.bilineata* *P. amentata*	Contact	Unknown*	2% effect(mortality,fertility) 0% 0% 0% 0%	N/A	1437574
Parasitic arthropod *A. rhopalosiphi*	Contact	Unknown*	75% (mortality, parasitism)	N/A	1437574
Birds					
Bobwhite quail	Acute	Flumioxazin	LD_{50} >2250 mg a.i./kg NOEL 2250 mg a.i./kg	Practicially non-toxic	1437816
	Dietary	Flumioxazin	LC_{50} >5620 mg a.i./kg diet NOEC 3160 mg a.i./kg diet	Practically non-toxic	1437819
	Reproduction	Flumioxazin	NOEC 500 mg a.i./kg diet	N/A	1437824
Mallard duck	Acute	Flumioxazin	LD_{50} >2250 mg a.i./kg	Practically non-toxic	1437574
	Dietary	Flumioxazin	LC_{50} >5620 mg a.i./kg diet NOEC 5620 mg a.i./kg diet	Practically non-toxic	1437821

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Reference
	Reproduction	Flumioxazin	NOEC 250 mg a.i./kg dw	N/A	1437827 1437829
Mammals					
Rat	Acute Oral	Flumioxazin	LD_{50} > 5000 mg a.i./kg bw	Practically non-toxic	1437547
	Acute Oral	Flumioxazin 51 WDG	LD_{50} > 5000 mg a.i./kg bw	Practically non-toxic	1437547
	90-Day Dietary	Flumioxazin	NOEL 69.7 mg a.i./kg dw (BWG)	N/A	1437547
	Multi-generational dietary (reproduction study)	Flumioxazin	NOEL 6.3 mg a.i./kg dw	N/A	1437547
	Developmental toxicity gavage	Flumioxazin	NOEL 3 mg a.i./kg dw Environmentally relevant NOEL 10 mg a.i./kg dw	N/A	1437547
Rabbit	Developmental toxicity gavage	Flumioxazin	NOEL 1000 mg a.i./kg dw	N/A	1437547
Vascular plants					
Vascular plant	Seedling emergence	Flumioxazin 51 WDG	EC_{25} = 0.90 g a.i./ha (lettuce) NOEC 0.45 g a.i./ha	N/A	1437842
	Vegetative vigour	Flumioxazin 51 WDG	EC_{25} = 0.09 g a.i./ha (cucumber) NOEC 0.054 g a.i./ha	N/A	1437846
			Species Sensitivity Distribution HC_5 of the EC_{50} values: 0.2732 g a.i./ha	N/A	

[a]Atkins et al. (1981) for bees and US EPA classification for others, where applicable
*Not submitted, but reviewed by another international regulatory agency

Table 11 Effects on Aquatic Organisms

Organism	Exposure	Endpoint value	Degree of toxicity[a]	Reference
Freshwater species				

Organism	Exposure	Endpoint value	Degree of toxicity[a]	Reference
Daphnia magna	Acute	EC_{50} = 5.9 mg a.i./L NOEC = 3.74 mg a.i./L	Moderately toxic	1437783 1437784
	Chronic	NOEC = 50.0 µg a.i./L (mortality and reproduction)		1437786
Rainbow trout	Acute	LC_{50} = 2.3 mg a.i./L NOEC = 0.92 mg a.i./L	Moderately toxic	1437800
	Chronic-juvenile growth	21-d NOEC: 0.37 mg a.i./L (not reviewed-EU endpoint)		1437804 1437574
	Chronic-ELS	NOEC = 0.0038 mg a.i./L		1437808 1437809 1437810 1437811
Bluegill sunfish	Acute	LC_{50} >21 mg a.i./L NOEC = 3.1 mg a.i./L	Slightly toxic	1437802
	Chronic	Study was not provided and is not required as the chronic rainbow trout ELS study has satisfied this data requirement.		
Freshwater alga *S. capricornutum* *A.flos-aqua* *N. pelliculosa*	Acute	 EC_{50} = 1.02 µg TR/L* EC_{50} = 0.83 µg TR/L EC_{50} = 1.4 µg TR/L*	Very highly toxic	1437838 1437834 1437836
Vascular plant	Dissolved	EC_{50} = 0.33 µg TR/L NOEC = 0.04 µg TR/L	Very highly toxic	1437848
	Over-spray	Study not provided, but is required. Given that flumioxazin is a contact herbicide and drift is a likely exposure scenario, an overspray study conducted with Flumioxazin 51 WDG is required to characterise the risk from drift and overspray to aquatic plants and algae. The analytical methodology used to confirm test concentrations should monitor both the parent compound and the major transformation products expected in water because of the instability of the parent in aquatic systems.		
Marine species				
Crustacean	Acute	LC_{50} = 0.23 mg a.i./L NOEC 0.072 mg a.i./L	Highly toxic	1437791
	Chronic*	NOEC 0.0015 mg a.i./L*	N/A	1437795
Mollusk	Acute	LC_{50} = 2.8 mg a.i./L NOEC <0.64 mg a.i./L	Moderately toxic	1437793
	Chronic	This study was not provided and is not required as the chronic daphnid study has satisfied this data requirement.		
Sheepshead minnow	Acute	LC_{50} >4.7 mg a.i./L NOEC 4.7 mg a.i./L	Moderately toxic	1437805
	Salinity challenge	No study was provided. This study is not required. On an acute basis, fish are less sensitive than aquatic vascular plants by a 10,000-fold difference. It is unlikely that a salinity challenge study would result in a more conservative aquatic endpoint than that provided by the aquatic vascular plant study.		
Marine alga	Acute	EC_{50} = 0.019 mg TR/L*	Very highly toxic	1437840
TR – Total Residue. The analytical method for the algae and aquatic vascular plants did not differentiate between parent and transformation				

Organism	Exposure	Endpoint value	Degree of toxicity[a]	Reference
products. The measured concentration was reflective of a total residue concentration. *- Study was not reviewed by PMRA. EPA endpoints are reported				

Table 12 Screening level risk assessment for Flumioxazin 51 WDG to terrestrial invertebrates

Organism	Exposure	Endpoint value	EEC	Risk	LOC Exceeded
Earthworm	Acute	LC_{50} ÷ 2: >491 mg a.i./kg dw	0.17 mg a.i./kg*	<0.01	No
Bee	Oral	LD_{50} > 100 µg a.i./bee equivalent to 112 kg a.i./ha (not reviewed by PMRA-EU endpoint)	0.391 kg a.i./ha	<0.01	No
	Contact	105 µ a.i./bee equivalent to 117.6 kg a.i./ha	0.391 kg a.i./ha	<0.01	No
	Brood / hive	Study not provided and is not required since flumioxazin was relatively non-toxic on a contact basis and the mode of action is not expected to affect the growth of juvenile bees.			
Typhlodromus pyri	Contact	Mortality, fertility: 2% (protonymphs; 50% WP, 0.6 kg a.s./ha)	0.391 kg a.i./ha	0.65	No
Aphidius rhopalosiphi	Contact	Mortality, parasitism: 75% (adults; 50% WP, 0.6 kg a.s/ha)	0.391 kg a.i./ha	N/A	Yes
Poecilus cupreus	Contact	Mortality: 0% (larvae; 50% WP, 0.6 kg a.s./ha)	0.391 kg a.i./ha	0.65	No
Chrysoperla carnea	Contact	Mortality: 0% (larvae; 50% WP, 0.6 kg a.s./ha)	0.391 kg a.i./ha	0.65	No
Aleochara bilineata	Contact	Reproduction: < 0% (adults; 50% WP, 0.6 kg a.s./ha)	0.391 kg a.i./ha	0.65	No
Pardosa amentata	Contact	Mortality, food consumption: 0% (adults; 50% WP, 0.6 kg a.s./ha)	0.391 kg a.i./ha	0.65	No

N/A Since a toxic effect was noted at the only test concentration tested which was 6x higher than the proposed application rate; a risk was identified even if a quotient could not be calculated.
Risk Quotient (RQ) = exposure/toxicity
Estimated Environmental Concentration (EEC)
Level of Concern (LOC)
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and or further characterisation where possible.

Table 13 Screening level risk assessment on non-target birds and mammals for Flumioxazin 51 WDG assuming an application rate of 2 x 214 g ai/ha, 30 day interval and assuming a 35-day foliar half-life between applications

Weight (kg)	Exposure	Endpoint value (mg a.i./kg bw/d)		Food guild	EDE[1] (mg a.i./ kg bw/d)	RQ[2]	Exceeds LOC[3]
Birds							
0.02	Acute	$LD_{50}/10$: >	225	Insectivore (small insects)	16.74	0.07	no
				Granivore	2.86	0.01	no
				Frugivore	8.63	0.04	no
	Dietary	5-d $LD_{50}/10$: >	171.1	Insectivore	16.74	0.10	no
				Granivore	2.86	0.02	no
				Frugivore	8.63	0.05	no
	Reproduction	NOEL:	34.93	Insectivore	16.74	0.48	no
				Granivore	2.86	0.08	no
				Frugivore	8.63	0.25	no
0.1	Acute	$LD_{50}/10$: >	225	Insectivore (small insects)	13.06	0.06	no
				Granivore	2.24	<0.01	no
				Frugivore	6.73	0.03	no
	Dietary	5-d $LD_{50}/10$: >	171.1	Insectivore		0.08	no
					13.06	<0.01	no
				Granivore	2.24	0.01	no
				Frugivore	6.73	0.04	no
	Reproduction	NOEL:	34.93	Insectivore		0.37	no
				(small insects)	13.06	<0.01	no
				Granivore	2.24	0.06	no
				Frugivore	6.73	0.19	no
1	Acute	$LD_{50}/10$: >	225	Insectivore (large insects)	0.65	<0.01	no
				Granivore	0.65	<0.01	no
				Frugivore	1.97	<0.01	no
				Herbivore		<0.01	no
				Short grass	13.63	0.06	no
				Long grass	8.32	0.04	no
				Forage crops	12.51	0.06	no
				Leafy foliage	23.77	0.11	no
	Dietary	5-d $LD_{50}/10$:>	171.1	Insectivore (large insects)	0.65	<0.01	no
				Granivore	0.65	<0.01	no
				Frugivore	1.97	0.01	no
				Herbivore		<0.01	no
				Short grass	13.63	0.08	no
				Long grass	8.32	0.05	no
				Forage crops	12.51	0.07	no
				Leafy foliage	23.77	0.14	no

Weight (kg)	Exposure	Endpoint value (mg a.i./kg bw/d)		Food guild	EDE[1] (mg a.i./ kg bw/d)	RQ[2]	Exceeds LOC[3]
	Reproduction	NOEL:	34.93	Insectivore (large insects)	0.065	<0.01	no
				Granivore	0.065	<0.01	no
				Frugivore	1.97	0.06	no
				Herbivore		<0.01	no
				Short grass	13.63	0.39	no
				Long grass	8.32	0.24	no
				Forage crops	12.51	0.36	no
				Leafy foliage	23.77	0.68	no
Mammals							
0.015	Acute	LD_{50}/10:	500	insectivore	9.63	0.02	no
				granivore	1.65	<0.01	no
				frugivore	4.96	<0.01	no
	Chronic	NOEL:	0.522	**insectivore**	**9.63**	**18.44**	**yes**
				granivore	**1.65**	**3.16**	**yes**
				frugivore	**4.96**	**9.51**	**yes**
0.035	Acute	LD_{50}/10:	500	insectivore (small insects)	8.44	0.02	no
				granivore	1.44	<0.01	no
				frugivore	4.35	<0.01	no
				short grass	30.16	0.06	no
				long grass	18.41	0.04	no
				forage crops	27.67	0.06	no
				leafy foliage	52.61	0.11	no
	Chronic	NOEL:	0.522	**insectivore (small insects)**	**8.44**	**16.17**	**yes**
				granivore	**1.44**	**2.77**	**yes**
				frugivore	**4.35**	**8.33**	**yes**
				short grass	**30.16**	**57.78**	**yes**
				long grass	**18.41**	**35.28**	**yes**
				forage crops	**27.67**	**53.01**	**yes**
				leafy foliage	**52.61**	**100.79**	**yes**
1	Acute	LD_{50}/10:	500	insectivores (larege insects)	0.77	<0.01	no
				granivore	0.77	<0.01	no
				frugivore	2.32	<0.01	no
				short grass	16.11	0.03	no
				long grass	9.84	0.02	no
				forage crops	14.79	0.03	no
				leafy foliage	28.11	0.06	no
	Chronic	NOEL:	0.522	**insectivores (large insects)**	**0.77**	**1.48**	**yes**
				granivore	**0.77**	**1.48**	**yes**
				frugivore	**2.32**	**4.45**	**yes**

Weight (kg)	Exposure	Endpoint value (mg a.i./kg bw/d)		Food guild	EDE[1] (mg a.i./ kg bw/d)	RQ[2]	Exceeds LOC[3]
				short grass	16.11	30.87	yes
				long grass	9.84	18.85	yes
				forage crops	14.79	28.33	yes
				leafy foliage	28.11	53.86	yes

[1]Estimated Daily Exposure (EDE) = FIRww/BW*EEC
Estimated Environmental Concentration (EEC) in fresh diet (mg a.i./kg fresh weight diet)
Food Ingestion Rate of indicator species in wet weight (FIR)
Bodyweight (BW) (kg);
[2]Risk Quotient (RQ) = exposure/toxicity
[3]Level of Concern (LOC)
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 14 Refinement of potential on-field risk to non-target mammals (Flumioxazin 51 WDG: 2 x 214 g ai/ha, 30 day interval and 10-day foliar half-life)

Weight (kg)	Exposure	Endpoint value (mg a.i./kg bw/day)		Food Guild	On Field		
					EDE[1]	RQ[2]	Exceeds LOC[3]
				insectivore	6.98	13.37	Yes
				granivore	1.19	2.29	Yes
0.015	Chronic	NOEL:	0.522	frugivore	3.60	6.89	Yes
				insectivore (small insects)	6.12	11.72	Yes
				granivore	1.05	2.00	Yes
				frugivore	3.15	6.04	Yes
				short grass	21.86	41.88	Yes
				long grass	13.35	25.57	Yes
				forage crops	20.06	38.43	Yes
0.035	Chronic	NOEL:	0.522	leafy foliage	38.14	73.06	Yes
				insectivores (large insects)	0.56	1.07	Yes
				granivore	0.56	1.07	Yes
				frugivore	1.68	3.23	Yes
				short grass	11.68	22.38	Yes
				long grass	7.13	13.66	Yes
				forage crops	10.72	20.53	Yes
1.00	Chronic	NOEL:	0.522	leafy foliage	20.38	39.04	Yes

[1]Estimated Daily Exposure (EDE) = FIRww/BW*EEC
Estimated Environmental Concentration (EEC) in fresh diet (mg a.i./kg fresh weight diet)
Food Ingestion Rate of indicator species in wet weight (FIR)
Bodyweight (BW) (kg);
[2]Risk Quotient (RQ) = exposure/toxicity
[3]Level of Concern (LOC)
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 15 Refined on-field and off-field risk assessment to non-target mammals (Flumioxazin 51 WDG: 2 x 214 g ai/ha, 30 day interval and 10-day foliar half-life) when used alone and when tankmixed with glyphosate.

Weight (kg)	Exposure	Endpoint value (mg a.i./kg bw/day)		Food Guild	On Field			Off Field		
					EDE	RQ	Exceeds LOC	EDE-6% Drift	RQ	Exceeds LOC
0.015	Chronic	NOEL:	0.522	insectivore	Exposure is not expected.[4]			0.42	0.80	No
				granivore	Exposure is not expected.[4]			0.07	0.14	No
				frugivore	Exposure is not expected.[4]			0.22	0.41	No
0.035	Chronic	NOEL:	0.522	insectivore (small insects)	Exposure is not expected.[4]			0.37	0.70	No
				granivore	Exposure is not expected.[4]			0.06	0.12	No
				frugivore	Exposure is not expected.[4]			0.19	0.36	No
				short grass	Exposure is not expected.[4]			1.31	2.51	Yes
				long grass				0.80	1.53	Yes
				forage crops				1.20	2.31	Yes
				leafy foliage				2.29	4.38	Yes
1.00	Chronic	NOEL:	0.522	insectivores (large insects)	Exposure is not expected.[4]			0.03	0.06	No
				granivore	Exposure is not expected.[4]			0.03	0.06	No
				frugivore	Exposure is not expected.[4]			0.10	0.19	No
				short grass	Exposure is not expected.[4]			**0.70**	**1.34**	**Yes**
				long grass				**0.43**	**0.82**	**No**
				forage crops				**0.64**	**1.23**	**Yes**
				leafy foliage				**1.22**	**2.34**	**Yes**

[1]Estimated Daily Exposure (EDE) = FIRww/BW*EEC
Estimated Environmental Concentration (EEC) in fresh diet (mg a.i./kg fresh weight diet); the off field EEC was used to refine exposure estimates. For off field EECs, the following deposition rates were used: 6% spray deposition: ground from ground boom application with a medium droplet spray quality (ASAE classification).
Food Ingestion Rate of indicator species in wet weight (FIR)
Bodyweight (BW) (kg);
[2]Risk Quotient (RQ) = exposure/toxicity
[3]Level of Concern (LOC)
[4]Exposure is not expected. Exposure is not expected based on the application method and/or the feeding behaviour of small mammals.
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 16 Screening level risk assessment on non-target terrestrial vascular plants (Flumioxazin 51 WDG: 2 x 214 g ai/ha, 30 day interval)

Organism	Exposure	Test Substance	Endpoint Value (g a.i./ha)		EEC[1] (g ai/ha)	RQ[2]	LOC[3] exceeded
Vascular plant	Seedling emergence	Flumioxazin 51 WDG	Monocot EC25:	4.1	391.45	95.48	yes
			Dicot EC25:	0.9	391.45	434.94	Yes
	Vegetative vigour	Flumioxazin 51 WDG	Monocot EC25:	6.72	332.15	49.43	Yes
			Dicot EC25:	0.09	332.15	3690.56	Yes

[1]Estimated Environmental Concentration (EEC) on foliage (vegetative vigour) and soil (seedling emergence) resulting from 2 applications of 214 g ai/ha (30-day interval and a 35-day half-life for foliage and a 111 day half life for soil.
[2]Risk Quotient (RQ) = exposure/toxicity
[3]Level of Concern (LOC)
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 17 On field and off field refined risk assessment on non-target terrestrial vascular plants (Flumioxazin 51 WDG: 2 x 214 g ai/ha, 30 day interval and 10-day foliar half-life for vegetative vigour and a 111 day half-life for seedling emergence

Organism	Exposure	Test Substance	Endpoint Value (g a.i./ha)		On Field			Off Field		
					EEC (g ai/ha)	RQ	LOC exceeded	EEC 6% Drift	RQ	LOC exceeded
Vascular plant	Seedling emergence	Flumioxazin 51 WDG	Monocot EC25:	4.1	391.45	95.48	yes	23.49	5.73	yes
			Dicot EC25:	0.9	391.45	434.94	yes	23.49	26.10	yes
	Vegetative vigour	Flumioxazin 51 WDG	Monocot EC25:	6.72	240.762	35.83	yes	14.45	2.15	yes
			Dicot EC25:	0.09	240.762	2675.13	yes	14.45	160.51	yes

[1]Estimated Environmental Concentration (EEC) on foliage (vegetative vigour) and soil (seedling emergence) resulting from 2 applications of 214 g ai/ha (30-day interval and a 10-day half-life for foliage and a 111 day half life for soil; the off-field EEC was used to refine exposure estimates. For off-field EECs, the following deposition rates were used: 6% spray deposition: ground from ground boom application with a medium droplet spray quality (ASAE classification).
[2]Risk Quotient (RQ) = exposure/toxicity
[3]Level of Concern (LOC)
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 18 On field and off field refined risk assessment on non-target terrestrial vascular plants (Flumioxazin 51 WDG: 2 x 214 g ai/ha, 30 day interval and 10-day foliar half-life) using the HC_5 of the EC_{50} values for all terrestrial plants tested.

Organism	Exposure	Test Substance	Endpoint Value[1] (g a.i./ha)		On Field			Off Field		
					EEC[2] (g ai/ha)	RQ[3]	LOC[4] exceeded	EEC[2] 6% Drift	RQ	LOC exceeded
Vascular plant	Vegetative vigour	Flumioxazin 51 WDG	HC5 of the EC50 values	0.273	240.762	881.27	yes	14.44572	52.88	yes

[1]The 5th percentile of the species sensitive distribution (HC5) for the EC50 at 50% confidence intervals was calculated, using the SSD program ETx2 (version 2.0), resulting at in 5% protection level.
[2]Estimated Environmental Concentration (EEC) on foliage (vegetative vigour) and soil (seedling emergence) resulting from 2 applications of 214 g ai/ha (30-day interval and a 10-day half-life for foliage and a 111 day half life for soil); the off-field EEC was used to refine exposure estimates. For off-field EECs, the following deposition rates were used: 6% spray deposition: ground from ground boom application with a medium droplet spray quality (ASAE classification).
[3]Risk Quotient (RQ) = exposure/toxicity
[4]Level of Concern (LOC)
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 19 Screening level risk assessment on non-target aquatic organisms (Flumioxazin 51 WDG) assuming an application rate of 2 x 214 g ai/ha and a 30 day interval between applications.

Organism	Exposure	Study Duration	Endpoint Value (mg a.i./L)		EEC[1] value	RQ[2]	LOC[3] exceeded
Freshwater Species							
Daphnid (*Daphnia magna*)	Acute (flow-through)	48 hours	LC50/2:	2.95	0.028	<0.01	no
	Chronic (flow-through)	21 days	NOEC	0.05	0.028	0.56	no
Rainbow Trout (*Onchorhynchus mykiss*)	Acute (flow-through)	96 hours	LC50/10:	0.23	0.028	0.12	no
	Chronic-ELS (flow-through)	87 days	NOEC	0.0077[4]	0.028	3.64	yes
	Chronic-Juvenile Growth (flow-through)	21 days	NOEC	0.37	0.028	0.08	no
Bluegill Sunfish (*Lepomis macrochirus*)	Acute	96 hours	LC50/10:	>2.1	0.028	<0.01	no
Green Algae (*Selenastrum capricornutum*)	Acute*	120 hours	LC50/2:	0.00051[4]	0.028	54.90	yes
Blue-green algae (*Anabaena flos-aqua*)	Acute	120 hours	LC50/2:	0.00042[4]	0.028	67.46	yes
Diatom (*Navicula pelliculosa*)	Acute	120 hours	LC50/2:	0.0007[4]	0.028	40.00	yes

Organism	Exposure	Study Duration	Endpoint Value (mg a.i./L)		EEC[1] value	RQ[2]	LOC[3] exceeded
Aquatic Vascular Plant (*Lemna gibba*)	Acute	14 days	LC50/2:	0.00017[4]	0.028	169.70	yes
Amphibians (15 cm depth)							
Amphibians	Acute[5]	96 hours	LC50/10:	0.23	0.148	0.65	no
	Chronic[5]	87 days	NOEC	0.0077	0.148	19.48	yes
Marine Species							
Mysid shrimp (*Mysidopsis bahia*)	Acute	96 hours	LC50/2:	0.115	0.028	0.24	no
	Chronic	28 days	NOEC	0.0015	0.028	18.67	yes
Eastern Oyster (*Crassostrea virginica*)	Acute	96 hours	LC50/2:	1.4	0.028	0.02	no
Sheepshead Minnow (*Cyprinodon variegatus*)	Acute	96 hours	LC50/10:	>0.47	0.028	<0.06	no
Diatom (*Skeletonema costatum*)	Acute	120 hours	LC50/2:	0.0095[4]	0.028	2.95	yes

[1]Estimated Environmental Concentration (EEC) on in water.
[2]Risk Quotient (RQ) = exposure/toxicity. For fish, RQ = EEC in an 80-cm deep water body / (EC50 ÷ 10 or LC50 ÷ 10); for a chronic exposure: RQ = EEC in an 80-cm deep water body / NOEC; for amphibians, the EEC in a 15 cm-deep water body is used. For aquatic invertebrates and plants, RQ = EEC in a 80-cm deep water body / (EC50 ÷ 2 or LC50 ÷ 2); for a chronic exposure: RQ = EEC in a 80-cm deep water body / NOEC
[3]Level of Concern (LOC)
[4]EPA or EU endpoint – study was not reviewed by PMRA. Analytical methods in the algal studies reported total radioactivity only, therefore concentrations are reported as total radioactivity (µg ^{14}C/L) instead of on an a.i. basis.
[5]the endpoint values for the most sensitive fish species at the appropriate exposure scenario were used as surrogate data for the amphibian risk assessment.
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 20 Refined risk assessment on non target aquatic organisms using Level 1 Drift values (Flumioxazin 51 WDG) assuming an application rate of 2 x 214 g ai/ha and a 30 day interval between applications

Species	Exposure	Study Duration	Endpoint value (mg a.i./L)		EEC[1] value	RQ[2]	LOC[3] Exceeded
Freshwater Species							
Daphnid (*Daphnia magna*)	Acute	48 hours	LC50/2:	2.95	0.00168	<0.01	no
	Chronic	21 days	NOEC	0.05	0.00168	0.03	no
Rainbow Trout (*Onchorhynchus mykiss*)	Acute	96 hours	LC50/10:	0.23	0.00168	0.01	no
	Chronic-ELS	87 days	NOEC	0.0077	0.00168	0.22	no
	Chronic-Juvenile Growth	21 days	NOEC	0.37	0.00168	<0.01	no
Bluegill Sunfish (*Lepomis macrochirus*)	Acute	96 hours	LC50/10:	2.1	0.00168	<0.01	no

Species	Exposure	Study Duration	Endpoint value (mg a.i./L)		EEC[1] value	RQ[2]	LOC[3] Exceeded
Green Algae (*Selenastrum capricornutum*)	Acute	120 hours	LC50/2:	0.00051[4]	0.00168	3.29	yes
Blue-green algae (*Anabaena flos-aqua*)	Acute	120 hours	LC50/2:	0.00042[4]	0.00168	4.05	yes
Diatom (*Navicula pelliculosa*)	Acute	120 hours	LC50/2:	0.0007[4]	0.00168	2.40	yes
Aquatic Vascular Plant (*Lemna gibba*)	Acute	14 days	LC50/2:	0.00017[4]	0.00168	10.18	yes
Amphibians (15 cm depth)							
Amphibians	Acute	96 hours	LC50/10:	0.23[5]	0.009	0.04	no
	Chronic	87 days	NOEC	0.0077[5]	0.009	1.17	yes
Marine Species							
Mysid shrimp (*Mysidopsis bahia*)	Acute	96 hours	LC50/2:	0.115	0.00168	0.01	no
	Chronic	28 days	NOEC	0.0015*	0.00168	1.12	yes
Eastern Oyster (*Crassostrea virginica*)	Acute	96 hours	LC50/2:	1.4	0.00168	<0.01	no
Sheepshead Minnow (*Cyprinodon variegatus*)	Acute	96 hours	LC50/10:	0.47	0.00168	<0.01	no
Diatom (*Skeletonema costatum*)	Acute	120 hours	LC50/2:	0.0095[4]	0.00168	0.18	no

[1]Estimated Environmental Concentration (EEC) on in water.
[2]Risk Quotient (RQ) = exposure/toxicity. For fish, RQ = EEC in an 80-cm deep water body / (EC50 ÷ 10 or LC50 ÷ 10); for a chronic exposure: RQ = EEC in an 80-cm deep water body / NOEC; for amphibians, the EEC in a 15 cm-deep water body is used. For aquatic invertebrates and plants, RQ = EEC in a 80-cm deep water body / (EC50 ÷ 2 or LC50 ÷ 2); for a chronic exposure: RQ = EEC in a 80-cm deep water body / NOEC
[3]Level of Concern (LOC)
[4]EPA or EU endpoint – study was not reviewed by PMRA. Analytical methods in the algal studies reported total radioactivity only, therefore concentrations are reported as total radioactivity (µg ^{14}C/L) instead of on an a.i. basis.
[5]the endpoint values for the most sensitive fish species at the appropriate exposure scenario were used as surrogate data for the amphibian risk assessment.
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 21 Refined risk assessment on non target aquatic organisms using Level 1 run-off values (Flumioxazin 51 WDG) assuming an application rate of 2 x 214 g ai/ha and a 30 day interval between applications

Species	Exposure	Study Duration	Endpoint value (mg a.i./L)		EEC[1] value	RQ[2]	Exceeds LOC[3]
Freshwater Species							
Daphnid (*Daphnia magna*)	Acute	48 hours	LC50/2:	2.95	0.01058	<0.01	no
	Chronic	21 days	NOEC	0.05	0.00052	0.01	no
Rainbow Trout (*Onchorhynchus mykiss*)	Acute	96 hours	LC50/10:	0.23	0.00255	0.01	no
	Chronic-ELS	87 days	NOEC	0.0077	0.00025	0.03	no
	Chronic-Juvenile Growth	21 days	NOEC	0.37[4]	0.00052	<0.01	no
Bluegill Sunfish (*Lepomis macrochirus*)	Acute	96 hours	LC50/10:	2.1	0.00255	<0.01	no
Green Algae (*Selenastrum capricornutum*)	Acute	120 hours	LC50/2:	0.00051[4]	0.00255	5.00	yes
Blue-green algae (*Anabaena flos-aqua*)	Acute	120 hours	LC50/2:	0.000415[4]	0.00255	6.14	yes
Diatom (*Navicula pelliculosa*)	Acute	120 hours	LC50/2:	0.0007[4]	0.00255	3.64	yes
Aquatic Vascular Plant (*Lemna gibba*)	Acute	14 days	LC50/2:	0.000165[4]	0.00255	15.45	yes
Amphibians (15 cm depth)							
Amphibians	Acute	96 hours	LC50/10:	0.23[5]	0.00987	0.04	no
	Chronic	87 days	NOEC	0.0077[5]	0.00101	0.13	no
Marine Species							
Mysid shrimp (*Mysidopsis bahia*)	Acute	96 hours	LC50/2:	0.115	0.00255	0.02	no
	Chronic	28 days	NOEC	0.0015	0.00052	0.35	no
Eastern Oyster (*Crassostrea virginica*)	Acute	96 hours	LC50/2:	1.4	0.00255	<0.01	no
Sheepshead Minnow (*Cyprinodon variegatus*)	Acute	96 hours	LC50/10:	0.47	0.00255	<0.01	no
Diatom (*Skeletonema costatum*)	Acute	120 hours	LC50/2:	0.0095[4]	0.00255	0.27	no

[1]Estimated Environmental Concentration (EEC) on in water.
[2]Risk Quotient (RQ) = exposure/toxicity. For fish, RQ = EEC in an 80-cm deep water body / (EC50 ÷ 10 or LC50 ÷ 10); for a chronic exposure: RQ = EEC in an 80-cm deep water body / NOEC; for amphibians, the EEC in a 15 cm-deep water body is used. For aquatic invertebrates and plants, RQ = EEC in a 80-cm deep water body / (EC50 ÷ 2 or LC50 ÷ 2); for a chronic exposure: RQ = EEC in a 80-cm deep water body / NOEC
[3]Level of Concern (LOC)
[4]EPA or EU endpoint – study was not reviewed by PMRA. Analytical methods in the algal studies reported total radioactivity only, therefore concentrations are reported as total radioactivity (µg ^{14}C/L) instead of on an a.i. basis.

Species	Exposure	Study Duration	Endpoint value (mg a.i./L)	EEC[1] value	RQ[2]	Exceeds LOC[3]
[5]the endpoint values for the most sensitive fish species at the appropriate exposure scenario were used as surrogate data for the amphibian risk assessment. Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.						

Table 22 Probability of exceedance characterisation for non-target aquatic organisms using modelled EEC run-off values (Flumioxazin 51 WDG) assuming an application rate of 2 x 214 g a.i./ha and a 30-day interval between applications.

Organism	Exposure	Test Substance	Endpoint value	Probablility of Exceeding the LOC[1]
Freshwater species				
Vascular plant (*Lemna gibba*)	Dissolved	^{14}C-Flumioxazin (static, total radioactivity measured, a.i. concentration not known)	96-h EC_{50}: 0.33 µg a.i./L 96-h EC_{50}/2: 0.165 µg a.i./L	87% chance of exceeding the LOC in a given year. This estimate is derived directly from the model output, showing that the endpoint of concern of 0.165 µg/L is exceeded in 87% of years based on a 50 year meteorological input file.
[1]LOC: level of concern Shaded cells indicate that the screening level risk quotient exceeds the level of concern, triggering a refined risk assessment.				

Table 23 Screening level risk assessment for Flumioxazin 0.25 G to terrestrial invertebrates

Organism	Exposure	Endpoint value	EEC[1]	RQ[2]	LOC[3] Exceeded
Earthworm	Acute	LC_{50} ÷ 2: >491 mg a.i./kg dw	0.34 mg a.i./kg	<0.01	No
Bee	Oral	Since Flumioxazin 0.25 G is a granular formulation to be applied directly to containers, exposure of bees as a result of pesticide residues or drift is unlikely to occur. The risk to these organisms was therefore not assessed.			
	Contact	Since Flumioxazin 0.25 G is a granular formulation to be applied directly to containers, exposure of bees as a result of pesticide residues or drift is unlikely to occur. The risk to these organisms was therefore not assessed.			
	Brood / hive	Study not provided and is not required since flumioxazin was relatively non-toxic on a contact basis and the mode of action is not expected to affect the growth of juvenile bees.			
Predators and Parasites	Contact	Since Flumioxazin 0.25 G is a granular formulation to be applied directly to containers, exposure of beneficials as a result of pesticide residues or drift is unlikely to occur. The risk to these organisms was therefore not assessed.			
[1]Estimated Environmental Concentration (EEC) [2]Risk Quotient (RQ) = exposure/toxicity [3]Level of Concern (LOC) Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and or further characterisation where possible.					

Table 24 Screening level granular risk assessment for terrestrial organisms[1] (Flumioxazin 0.25 G)

Species and body weight	Toxicity test exposure	Toxicity Endpoint	
		Screening Level Dose mg a.i./kg bw; mg a.i./kg bw/day	**Toxicity Endpoint expressed as: # granules to reach toxicity endpoint[2]**
small bird (20 g) (0.020 kg)	Acute oral-single dose	LD_{50}/10: > 225	> 3214 granules
	5-day dietary	5-d LD_{50}/10: > 171.1	>2444 granules/day
	Reproduction	NOEL: 34.93	498 granules/day
medium bird (100 g) (0.10 kg)	Acute oral-single dose	LD_{50}/10: > 225	> 16,071 granules
	5-day dietary	5-d LD_{50}/10: > 171.1	12,221 granules
	Reproduction	NOEL: 34.93	2488 granules/day
large bird (1000 g) (1 kg)	Acute oral-single dose	LD_{50}/10: > 225	> 160,714 granules
	5-day dietary	5-d LD_{50}/10: > 171.1	> 122,214 granules/day
	Reproduction	NOEL: 34.93	24,878 granules/day
small mammal (15 g) (0.015 kg)	Acute oral-single dose	1/10 LD_{50}: >500	> 5,357 granules
	Reproduction	NOEL: 0.522	5 granules/day
medium mammal (35 g) (0.035 kg)	Acute oral-single dose	1/10 LD_{50}: >500	> 12,500
	Reproduction	NOEL: 0.522	13 granules/day
large mammal (1000 g) (1 kg)	Acute oral-single dose	1/10 LD_{50}: >500	>357,142 granules
	Reproduction	NOEL: 0.522	372 granules/day

[1]The Flumioxazin 0.25 G risk assessment for birds and mammals is reported in this table.

[2]#granules/day = Toxicity dose / mg a.i./seed x BW (where the mg a.i./seed is 0.0014 mg a.i./granule)

Table 25 Screening level risk assessment on non-target aquatic organisms (Flumioxazin 0.25 G) assuming an application rate of 2 x 420 g ai/ha and a 30 day interval between appliations.

Organism	Exposure	Test Substance	Endpoint value (mg a.i./L)	EEC[1] (mg a.i./L)	RQ[2]	Exceeds LOC[3]
Freshwater species						
Daphnia	Acute (flow-through)	Flumioxazin	EC_{50}/2: 2.95	0.0544	0.02	No
	Chronic (flow-through)	Flumioxazin	21-day NOEC: 0.05	0.0544	1.09	Yes
Rainbow trout	Acute	Flumioxazin (flow-through)	LC_{50}/10: 0.23	0.0544	0.24	No
	Chronic –ELS	Flumioxazin (flow-through)	87-d NOEC: 0.0077	0.0544	7.06	Yes
	Chronic –juvenile growth	Flumioxazin (flow-through)	21-d NOEC: 0.37[4]	0.0544	0.15	No
Bluegill sunfish	Acute	Flumioxazin	96-h LC_{50}/10: >2.1	0.0544	0.03	No
Green algae (*Selenastrum capricornutum*)	Acute	^{14}C-Flumioxazin	96-h EC_{50}/2: 0.00051[4]	0.0544	106.67	Yes
Blue-green algae (*Anabaena flos-aqua*)	Acute	^{14}C-Flumioxazin	96-h EC_{50}/2: 0.00042[4]	0.0544	131.08	Yes
Diatom (*Navicula pelliculosa*)	Acute	^{14}C-Flumioxazin	96-h EC_{50}/2: 0.0007[4]	0.0544	77.71	Yes
Vascular plant (*Lemna gibba*)	Dissolved	^{14}C-Flumioxazin	96-h EC_{50}/2: 0.00017[4]	0.0544	329.70	Yes
Amphibians (15 cm depth)						
Amphibians	Acute (based on acute fish studies)	Flumioxazin (flow-through)	96-h LC_{50}/10: 0.23[5]	0.0290	1.26	Yes
	Chronic (based on early life stage fish study)	Flumioxazin (flow-through)	87-d NOEC: 0.0077	0.0290	37.66	Yes
Marine species						
Mysid shrimp	Acute	Flumioxazin (flow-through)	96-h LC_{50}/10: 0.023	0.0544	0.47	No
	Chronic	Flumioxazin (flow-through)	NOEC: 0.0015 [4]	0.0544	36.27	Yes
Eastern oyster	Acute	Flumioxazin	96-h LC_{50}/10: 0.28	0.0544	0.04	No
Sheepshead minnow	Acute	Flumioxazin (flow-through)	96-h LC_{50}/10: >0.47	0.0544	0.12	No
Diatom (*Skeletonema costatum*)	Acute	Flumioxazin (static)	96-h LC_{50}/10:0.0019[4]	0.0544	5.73	Yes

[1]Estimated Environmental Concentration (EEC) on in water.
[2]Risk Quotient (RQ) = exposure/toxicity. For fish, RQ = EEC in an 80-cm deep water body / (EC50 ÷ 10 or LC50 ÷ 10); for a chronic exposure: RQ = EEC in an 80-cm deep water body / NOEC; for amphibians, the EEC in a 15 cm-deep water body is used. For aquatic invertebrates and plants, RQ = EEC in a 80-cm deep water body / (EC50 ÷ 2 or LC50 ÷ 2); for a chronic exposure: RQ = EEC in a 80-cm deep water body / NOEC
[3]Level of Concern (LOC)
[4]EPA or EU endpoint – study was not reviewed by PMRA. Analytical methods in the algal studies reported total radioactivity only, therefore concentrations are reported as total radioactivity (µg ^{14}C/L) instead of on an a.i. basis.
[5]the endpoint values for the most sensitive fish species at the appropriate exposure scenario were used as surrogate data for the amphibian risk assessment.
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 26 Refined risk assessment on non target aquatic organisms using Level 1 run-off values (Flumioxazin 0.25 G) assuming an application rate of 2 x 420 g ai/ha and a 30 day interval between applications

Species	Exposure	Study Duration	Endpoint value (mg a.i./L)		EEC[1] value	RQ[2]	Exceeds LOC[3]
Freshwater Species							
Daphnid (*Daphnia magna*)	Acute	48 hours	LC50/2:	2.95	0.0208	<0.01	no
	Chronic	21 days	NOEC	0.05	0.00101	0.02	no
Rainbow Trout (*Onchorhynchus mykiss*)	Acute	96 hours	LC50/10:	0.23	0.00501	0.02	no
	Chronic-ELS	87 days	NOEC	0.0077	0.000491	0.06	no
	Chronic-Juvenile Growth	21 days	NOEC	0.37[4]	0.00101	<0.01	no
Bluegill Sunfish (*Lepomis macrochirus*)	Acute	96 hours	LC50/10:	2.1	0.00501	<0.01	no
Green Algae (*Selenastrum capricornutum*)	Acute	120 hours	LC50/2:	0.00051[4]	0.00501	9.82	yes
Blue-green algae (*Anabaena flos-aqua*)	Acute	120 hours	LC50/2:	0.000415[4]	0.00501	12.07	yes
Diatom (*Navicula pelliculosa*)	Acute	120 hours	LC50/2:	0.0007[4]	0.00501	7.16	yes
Aquatic Vascular Plant (*Lemna gibba*)	Acute	14 days	LC50/2:	0.000165[4]	0.00501	30.36	yes
Amphibians (15 cm depth)							
Amphibians	Acute	96 hours	LC50/10:	0.23[5]	0.0194	0.08	no
	Chronic	87 days	NOEC	0.0077[5]	0.00198	0.26	no
Marine Species							
Mysid shrimp (*Mysidopsis bahia*)	Acute	96 hours	LC50/2:	0.115	0.00501	0.04	no
	Chronic	28 days	NOEC	0.0015[4]	0.00101	0.67	no
Eastern Oyster (*Crassostrea virginica*)	Acute	96 hours	LC50/2:	1.4	0.00501	<0.01	no
Sheepshead Minnow (*Cyprinodon variegatus*)	Acute	96 hours	LC50/10:	0.47	0.00501	0.01	no
Diatom (*Skeletonema costatum*)	Acute	120 hours	LC50/2:	0.0095[4]	0.00501	0.53	no

[1]Estimated Environmental Concentration (EEC) on in water.
[2]Risk Quotient (RQ) = exposure/toxicity. For fish, RQ = EEC in an 80-cm deep water body / (EC50 ÷ 10 or LC50 ÷ 10); for a chronic exposure: RQ = EEC in an 80-cm deep water body / NOEC; for amphibians, the EEC in a 15 cm-deep water body is used. For aquatic invertebrates and plants, RQ = EEC in a 80-cm deep water body / (EC50 ÷ 2 or LC50 ÷ 2); for a chronic exposure: RQ = EEC in a 80-cm deep water body / NOEC
[3]Level of Concern (LOC)
[4]EPA or EU endpoint – study was not reviewed by PMRA. Analytical methods in the algal studies reported total radioactivity only, therefore concentrations are reported as total radioactivity (µg ^{14}C/L) instead of on an a.i. basis.
[5]the endpoint values for the most sensitive fish species at the appropriate exposure scenario were used as surrogate data for the amphibian risk assessment.
Shadded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 27 Probability of exceedance characterisation for non-target aquatic organisms using modelled EEC run-off values (Flumioxazin 0.25G) assuming an application rate of 2 x 420 g a.i./ha and a 30-day interval between applications.

Organism	Exposure	Test Substance	Endpoint value	Probablility of Exceeding the LOC[1]
Freshwater species				
Vascular plant (*Lemna gibba*)	Dissolved	^{14}C-Flumioxazin (static, total radioactivity measured, a.i. concentration not known)	96-h EC_{50}: 0.33 µg a.i./L 96-h EC_{50}/2: 0.165 µg a.i./L	100% chance of exceeding the LOC in a given year. This estimate is derived directly from the model output, showing that the endpoint of concern of 0.165 µg/L is exceeded in 100% of years based on a 50 year meteorological input file.

[1]LOC: level of concern
Shaded cells indicate that the screening level risk quotient exceeds the level of concern, triggering a refined risk assessment.

Table 28 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoint	Transformation Products Endpoint
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes	Yes
Predominantly anthropogenic[2]	Yes		Yes	Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	13.1 to 110.9 days in aerobic soil	Limited information was provided on the chemistry and fate of the flumioxazin transformation products. The laboratory studies indicated that several major transformation products (482-HA, APF, THPA, HPA, SAT-482-HA, SAT-482-HA-2, DAPF) accumulate under hydrolysis and anaerobic aquatic conditions.
	Water	Half-life ≥ 182 days	9.0 to 9.8 hours in anaearobic soil water system	
	Sediment	Half-life ≥ 365 days	1.1 to 1.4 days in anaerobic aquatic sediment system.	
	Air	Half-life ≥ 2 days or evidence of long range transport	Flumioxazin does not meet the Track 1 criterion for persistence in air because volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on its vapour pressure (3.21 x 10^{-4} Pa) and Henry's Law constant (6.252 x 10^{-7} atm·m^3/mol).	

TSMP Track 1 Criteria	TSMP Track 1 Criterion value	Active Ingredient Endpoint	Transformation Products Endpoint
Bioaccumulative[4]	Log $K_{OW} \geq 5$	2.55	Not available. Log K_{OW} information is required to determine whether they meet the TSMP criteria for bioaccumulation.
	BCF $\geq$ 5000	Not available	Not available
	BAF $\geq$ 5000	Not available	Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?		No, does not meet TSMP Track 1 criteria.	No, does not meet TSMP Track 1 criteria.

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e., all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]Field data (e.g., BAFs) are preferred over laboratory data (e.g., BCFs) which, in turn, are preferred over chemical properties (e.g., log K_{OW}).

Table 29 Weed (FLUMIOXAZIN 51WDG Herbicide label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Applicant Proposed Weed Claims	Accepted Weed Claims	Unsupported Weed Claims
redroot pigweed, green pigweed, palmer amaranth, smooth pigweed, tall waterhemp, common waterhemp, velvetleaf, common ragweed, shepherd's-purse, hairy bittercress, mouse-eared chickweed, common lamb's-quarters, large crabgrass, barnyardgrass, Canada fleabane, spotted spurge, henbit, kochia, common mallow, round-leaved mallow, liverwort, yellow woodsorrel, witchgrass, fall panicum, narrow-leaved plantain, broad-leaved plantain, annual bluegrass, lady's-thumb, green smartweed, common purslane, Russian thistle, common groundsel, giant foxtail, yellow foxtail, green foxtail, wild mustard, black nightshade, Eastern black nightshade, hairy nightshade, annual sowthistle, common chickweed, dandelion, stinkweed, giant ragweed (suppression only), and wild buckwheat (suppression only)	common lamb's-quarters, redroot pigweed, common ragweed, green pigweed, eastern black nightshade, hairy nightshade, green foxtail, and dandelion	palmer amaranth, smooth pigweed, tall waterhemp, common waterhemp, velvetleaf, shepherd's-purse, hairy bittercress, mouse-eared chickweed, large crabgrass, barnyardgrass, Canada fleabane, spotted spurge, henbit, kochia, common mallow, round-leaved mallow, liverwort, yellow woodsorrel, witchgrass, fall panicum, narrow-leaved plantain, broad-leaved plantain, annual bluegrass, lady's-thumb, green smartweed, common purslane, Russian thistle, common groundsel, giant foxtail, yellow foxtail, wild mustard, black nightshade, annual sowthistle, common chickweed, stinkweed, giant ragweed (suppression only), and wild buckwheat (suppression only)

Table 30 Use (FLUMIOXAZIN 51WDG Herbicide label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Applicant Proposed Use Claims	Accepted Use Claims	Unsupported Use Claims
bare ground non-crop area	bare ground non-crop area	
soybean	soybean	
field-grown deciduous ornamental trees (apple spp., apricot spp., ash spp., birch spp., cherry spp., chestnut spp., dogwood spp., eucalyptus spp., gingko spp., lilac spp., maple spp., crape myrtle, oak spp., poplar spp., peach spp., pear spp., plum spp., redbud, sweetgum, sycamore spp, black walnut, and willow spp.)	field-grown deciduous ornamental trees* (green ash, Japanese lilac, and Norway maple)	field-grown deciduous ornamental trees** (apple spp., apricot spp., ash spp., birch spp., cherry spp., chestnut spp., dogwood spp., eucalyptus spp., gingko spp., lilac spp., maple spp., crape myrtle, oak spp., poplar spp., peach spp., pear spp., plum spp., redbud, sweetgum, sycamore spp, black walnut, and willow spp.)
field-grown coniferous ornamental trees including Christmas trees and trees produced for reforestation (American arborvitae, Douglas fir, balsam fir, Fraser fir, grand fir, Noble fir, Eastern hemlock, Western hemlock, blue star juniper, creeping juniper, Japanese garden juniper, tamarix, Eastern white pine, jack pine, loblolly pine, lodgepole pine, longleaf pine, ponderosa pine, sand pine, Scotch pine, shortleaf pine, slash pine, Virginia pine, blue spruce, dwarf Alberta spruce, Norway spruce, sitka spruce, English yew, and Japanese yew)	field-grown coniferous ornamental trees including Christmas trees and trees produced for reforestation (American arborvitae, Douglas fir, balsam fir, Fraser fir, and blue spruce)	field-grown coniferous ornamental trees including Christmas trees and trees produced for reforestation** (grand fir, Noble fir, Eastern hemlock, Western hemlock, blue star juniper, creeping juniper, Japanese garden juniper, tamarix, Eastern white pine, jack pine, loblolly pine, lodgepole pine, longleaf pine, ponderosa pine, sand pine, Scotch pine, shortleaf pine, slash pine, Virginia pine, dwarf Alberta spruce, Norway spruce, sitka spruce, English yew, and Japanese yew)
dry-bulb onions	dry-bulb onions	
potato	potato	
sweet potato		sweet potato
pome fruit (apple and pear)	pome fruit (apple and pear)	
grape	grape	
strawberry	strawberry***	
asparagus	asparagus	
highbush blueberry	highbush blueberry	
stone fruit (peach, cherry, nectarine, plum and apricot)	stone fruit (peach, cherry, nectarine, plum and apricot)	

*: Consult section on POME FRUIT and STONE FRUIT for the list of tolerant species, specific use directions and restrictions.

**: Only ornamental species listed on the label have shown tolerance to this product. However, a warning statement regarding species not listed does appear on the label. This warning statement provides instructions for conducting a bioassay on non-listed species.

***: Tolerance of strawberry to this product has not been established. A warning statement appears on the label advising of potential crop injury and yield loss.

Table 31 Weed (FLUMIOXAZIN 0.25G Herbicide label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Applicant Proposed Weed Claims	Accepted Weed Claims	Unsupported Weed Claims
redroot pigweed, green pigweed, palmer amaranth, smooth pigweed, tall waterhemp, common waterhemp, velvetleaf, common ragweed, shepherd's-purse, hairy bittercress/snapweed, mouse-eared chickweed, common chickweed, common lamb's-quarters, Canada fleabane, spotted spurge, henbit, kochia, common mallow, round-leaved mallow, liverwort, pearlwort, yellow woodsorrel, narrow-leaved plantain, broad-leaved plantain, lady's-thumb, green smartweed, common purslane, Russian thistle, common groundsel, wild mustard, black nightshade, Eastern black nightshade, hairy nightshade, annual sowthistle, dandelion, stinkweed, large crabgrass, barnyardgrass, giant foxtail, yellow foxtail, green foxtail, witchgrass, fall panicum, annual bluegrass, giant ragweed (suppression only), and wild buckwheat (suppression only)	hairy bittercress/snapweed, liverwort, common groundsel (suppression only) and common chickweed (suppression only)	redroot pigweed, green pigweed, palmer amaranth, smooth pigweed, tall waterhemp, common waterhemp, velvetleaf, common ragweed, shepherd's-purse, mouse-eared chickweed, common lamb's-quarters, Canada fleabane, spotted spurge, henbit, kochia, common mallow, round-leaved mallow, pearlwort, yellow woodsorrel, narrow-leaved plantain, broad-leaved plantain, lady's-thumb, green smartweed, common purslane, Russian thistle, wild mustard, black nightshade, Eastern black nightshade, hairy nightshade, annual sowthistle, dandelion, stinkweed, large crabgrass, barnyardgrass, giant foxtail, yellow foxtail, green foxtail, witchgrass, fall panicum, annual bluegrass, giant ragweed (suppression only), and wild buckwheat (suppression only)

Table 32 Use (FLUMIOXAZIN 0.25G Herbicide label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Applicant Proposed Use Claims	Accepted Use Claims	Unsupported Use Claims
container-grown ornamental trees (American arborvitae, Giant arborvitae, Oriental arborvitae, ash spp., green ash, white ash, birch spp., deodora cedar, flowering crabapple, cottonwood, cottonwood, Italian cypress, templeoff cypress, Florida dogwood, Siberian dogwood, Chinese elm, mealy eucalyptus, red gum eucalyptus, ficus, balsam fir, Douglas fir, Fraser fir, grand fir, Korean fir, noble fir, ginkgo, Eastern hemlock, mountain hemlock, Western hemlock, lilac spp., Hungarian lilac, lily magnolia, maple spp., flame maple, flowering maple, Japanese maple, red maple, striped maple, white mulberry, bear oak, live oak, pin oak, red oak, willow oak, Eastern white pine, jack pine, lacebark pine, loblolly pine, lodgepole pine, longleaf pine, mugo pine, ponderosa pine, sand pine, scotch pine, shortleaf pine, slash pine, Virginia pine, beach plum, podocarpus spp., poplar spp.,	container-grown ornamental trees (American arborvitae, flame maple, Japanese maple, red oak, blue spruce, white spruce, and yew)	container-grown ornamental trees** (Giant arborvitae, Oriental arborvitae, ash spp., green ash, white ash, birch spp., deodora cedar, flowering crabapple, cottonwood, cottonwood, Italian cypress, templeoff cypress, Florida dogwood, Siberian dogwood, Chinese elm, mealy eucalyptus, red gum eucalyptus, ficus, balsam fir, Douglas fir, Fraser fir, grand fir, Korean fir, noble fir, ginkgo, Eastern hemlock, mountain hemlock, Western hemlock, lilac spp., Hungarian lilac, lily magnolia, maple spp., flowering maple, red maple, striped maple, white mulberry, bear oak, live oak, pin oak, willow oak, Eastern white pine, jack pine, lacebark pine, loblolly pine, lodgepole pine, longleaf pine, mugo pine, ponderosa pine, sand pine, scotch pine, shortleaf pine, slash pine, Virginia pine, beach plum, podocarpus spp., poplar spp., Eastern red cedar, redbud, spruce

Applicant Proposed Use Claims	Accepted Use Claims	Unsupported Use Claims
Eastern red cedar, redbud, spruce spp., blue spruce, dwarf Alberta spruce, Norway spruce, Serbian spruce, sitka spruce, staghorn sumac, American sweetgum, American sycamore, California sycamore, Japanese yew, and yew)		spp., dwarf Alberta spruce, Norway spruce, Serbian spruce, sitka spruce, staghorn sumac, American sweetgum, American sycamore, California sycamore, and Japanese yew)
container-grown ornamental shrubs and ground covers (glossy abelia, acacia spp., purple anise, azalea spp., barberry spp., Japanese barberry, William Penn barberry, bayberry, bottlebrush, boxwood spp., littleleaf boxwood, camellia, shrubby cinquefoil, bearberry cotoneaster, myrtle crape, Elaeagnus spp., English ivy, winged euonymous, scarlet firethorn, border forsythia, weeping forsythia, white, forsythia, cape jasmine gardenia, heath, Chinese holly, inkberry holly, Japanese holly, meserve holly, Nellie R. Stevens holly, Japanese honeysuckle, Indian hawthorn, juniper spp., creeping juniper, shore juniper, singleseed juniper, myoporum, oleander spp., Oregon grape, pachysandra, photinia, Japanese pieris, Japanese pittosporum, Chinese pittosporum, pyracantha spp., catawba rhododendron, rose spp., spirea spp., sweet flag, Virginia sweetspire, tea olive, viburnum spp., arrowwood viburnum, pink dawn viburnum, sweet viburnum, weigela)	container-grown ornamental shrubs and ground covers (common boxwood, creeping juniper, and savin juniper)	container-grown ornamental shrubs and ground covers** (glossy abelia, acacia spp., purple anise, azalea spp., barberry spp., Japanese barberry, William Penn barberry, bayberry, bottlebrush, boxwood spp., littleleaf boxwood, camellia, shrubby cinquefoil, bearberry cotoneaster, myrtle crape, Elaeagnus spp., English ivy, winged euonymous, scarlet firethorn, border forsythia, weeping forsythia, white, forsythia, cape jasmine gardenia, heath, Chinese holly, inkberry holly, Japanese holly, meserve holly, Nellie R. Stevens holly, Japanese honeysuckle, Indian hawthorn, juniper spp., shore juniper, singleseed juniper, myoporum, oleander spp., Oregon grape, pachysandra, photinia, Japanese pieris, Japanese pittosporum, Chinese pittosporum, pyracantha spp., catawba rhododendron, rose spp., spirea spp., sweet flag, Virginia sweetspire, tea olive, viburnum spp., arrowwood viburnum, pink dawn viburnum, sweet viburnum, weigela)

Applicant Proposed Use Claims	Accepted Use Claims	Unsupported Use Claims
container-grown non-bearing fruit and nut trees and vines (apple spp., huckleberry blueberry, bramble spp., sweet cherry, grape spp., peach, pear, prune spp., stone fruit, walnut spp., chestnut spp., pecan, pistachio, almond, and filbert)		container-grown non-bearing fruit and nut trees and vines** (apple spp., huckleberry blueberry, bramble spp., sweet cherry, grape spp., peach, pear, prune spp., stone fruit, walnut spp., chestnut spp., pecan, pistachio, almond, and filbert)

**: Only ornamental species listed on the label have shown tolerance to this product. However, a warning statement regarding species not listed does appear on the label. This warning statement provides instructions for conducting a bioassay on non-listed species.

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

Canadian raw agricultural commodity (RAC) MRLs are the same as the American RAC MRLs. No Codex MRLs have been established.

Crop Groups: Numbers and Definitions

Crop Group Number	Name of the Crop Group	Commodity
1C	Tuberous and Corm Vegetables	arracacha arrowroot Chinese artichokes Jerusalem artichokes edible canna cassava roots chayote roots chufa taro corms ginger roots lerens potatoes sweet potato roots tanier corms turmeric roots yam bean roots true yam tubers
3-07A	Bulb Onion Subgroup	garlic great-headed garlic dry bulb onions shallot bulbs potato onions daylilies fritillaria bulbs serpent garlic lilies Chinese onions pearl onions
11	Pome Fruit	apples crabapples loquats mayhaws pears oriental pears quinces
12	Stone Fruits	apricots sweet cherries tart cherries nectarines peaches plums plumcots prune plums

Crop Group Number	Name of the Crop Group	Commodity
13-07B	Bushberry	highbush blueberries lowbush blueberries currants elderberries gooseberries huckleberries Aronia berries Buffalo currants Chilean guava European barberries highbush cranberries honeysuckle jostaberries Saskatoon berries (juneberries) lingonberries native currants salal berries sea buckthorn
13-07F	Small fruit vine climbing, except fuzzy kiwifruit	gooseberries Amur river grapes grapes hardy kiwifruit maypop Schisandra berries
13-07G	Low growing berry subgroup	lowbush blueberries bearberries bilberries cloudberries cranberries lingonberries muntries partridgeberries strawberries

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

2.0 Human and Animal Health

3.0 Environment

4.0 Value

B. Additional Information Considered

i) Published Information

1.0 Chemistry

2.0 Human and Animal Health

3.0 Environment

4.0 Value

ii) Unpublished Information

1.0 Chemistry

2.0 Human and Animal Health

3.0 Environment

4.0 Value